

From: [Das, Abhik](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: SUPPORT Growth
Date: Thursday, June 17, 2010 12:17:05 PM

Should we contact Shahnaz to get started on this?

Abhik Das, Ph.D.

Senior Research Statistician

RTI International

6110 Executive Blvd., Suite 902

Rockville, MD 20852-3903

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Phone: 301-770-8214

Fax: 301-230-4646

From: Bell, Edward
To: Johnson, Karen; Acarregui, Michael; Eastman, Diane
Cc: mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Follow Up
Date: Friday, June 11, 2010 3:33:07 PM

Well done, Diane and Mike! Thanks for your strong work.
Ed

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, June 11, 2010 1:37 PM
To: Bell, Edward; Johnson, Karen; Acarregui, Michael; Eastman, Diane
Cc: mgantz@rti.org
Subject: SUPPORT Follow Up

Congratulations!!
We have no currently missing SUPPORT Follow up
Data from your site. Keep up the good work and
thanks for all the effort!!!
Rose

Rosemary D. Higgins, MD
Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research Network
Pregnancy and Perinatology Branch
CDBPM, NIH
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-435-7909
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Cunningham, Meg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: Support_Secondary_Analyses20100607
Date: Friday, June 11, 2010 10:33:36 AM

Do you have an email address for LeVan?

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, June 11, 2010 9:57 AM
To: Zaterka-Baxter, Kristin; Cunningham, Meg
Subject: Support_Secondary_Analyses20100607

Sorry for the delay – minor suggestions.

Can you also send a copy to each of the folks that submitted proposals (Luc Brion, Duke folks) alerting them to their reviews?

thanks
Rose

From: [Cunningham, Meg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#); [Zaterka-Baxter, Kristin](#)
Subject: RE: Support_Secondary_Analyses20100607
Date: Friday, June 11, 2010 10:02:00 AM

Will do. I will send the reviews out separately and then post the minutes on the website.

Thanks!

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, June 11, 2010 9:57 AM
To: Zaterka-Baxter, Kristin; Cunningham, Meg
Subject: Support_Secondary_Analyses20100607

Sorry for the delay – minor suggestions.

Can you also send a copy to each of the folks that submitted proposals (Luc Brion, Duke folks) alerting them to their reviews?

thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Rich, Wade"; "Finer, Neil"
Subject: RE: Pediatrics - 2009-3353.R2
Date: Wednesday, May 26, 2010 1:32:00 PM

Congratulations!!
Very nice - early release!!

-----Original Message-----

From: Rich, Wade [mailto:wrich@ucsd.edu]
Sent: Wednesday, May 26, 2010 1:27 PM
To: Finer, Neil
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Pediatrics - 2009-3353.R2

Fyi

wade

-----Original Message-----

From: onbehalfof+martha.andreas+uvm.edu@manuscriptcentral.com
[mailto:onbehalfof+martha.andreas+uvm.edu@manuscriptcentral.com] On Behalf Of martha.andreas@uvm.edu
Sent: Wednesday, May 26, 2010 8:49 AM
To: Rich, Wade
Subject: Pediatrics - 2009-3353.R2

26-May-2010

RE: 2009-3353.R2 - Antenatal consent in a trial of immediate neonatal management: Challenges, costs and representative enrollment

Dear Mr. Rich:

Pediatrics is pleased to announce the early release of your article in eFirst pages on June 28. This will be your definitive publication date. The media embargo will lift at 12:01 a.m. ET on the day of publication.

Under the title of each online article, you will see a string like this: doi: 10.1542/peds.2008-1536 This is the Digital Object Identifier (DOI) number; the doi follows the life of an article.

Articles can be cited using the DOI. For more information on using DOIs to cite articles, visit www.doi.org.

To cite your online, published ahead of print article, use this format:

Author(s), Article Title, Pediatrics published online: date (doi: 10.1542/peds.year.4-digit number)

Congratulations on your forthcoming publication.

Sincerely,

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Houston office at (832) 824-1166 between 9:00 a.m. and 4:00 p.m. CST, Monday thru Friday.

From: Susan Hintz
To: kristin.zaterka
Cc: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: Late Breaker presentation
Date: Friday, May 21, 2010 4:06:58 PM
Attachments: Hintz_SUPPORT_NEURO_CUS_PAS2010.ppt

Hi all,

I was looking up an abstract from NRN on the website, and saw that the SUPPORT NEURO CUS analysis late breaker presentation was not among the PAS 2010 presentations. In case you don't have a copy, here it is attached.

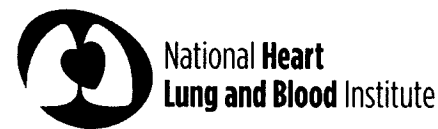
Thanks

Susan



Early and Late CUS Findings in the SUPPORT Neuroimaging and Neurodevelopmental Outcomes (NEURO) Cohort

SR Hintz, D Bulas, TL Slovis, H Cheng, N Finer, A Das,
RD Higgins, SUPPORT Subcommittee, for NICHD
Neonatal Research Network



Disclosure

- The presenter, Susan R. Hintz, M.D., has no conflicts to disclose



Cranial US

- Cranial US is a crucial neuroimaging tool, current standard of care for preterm infants.
 - Ment LR, et. al. *Neurology* 2002; 58:1726
- CUS findings are used to assist in prognosis of neurodevelopmental outcomes.
- Data regarding CUS findings and childhood outcomes in recent extremely preterm cohorts are essential.
 - O'Shea TM, et. al. *Pediatrics* 2008;122:e662; Kuban KCK, et. al. *J Child Neurol* 2009;24:63



Objective

- In the NEURO subcohort of the NICHD Neonatal Research Network Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT), we determined:
 - **Early and late CUS findings**
 - **Inter-rater reliability between central readers**
 - **Accuracy of local readings compared with central readings**



SUPPORT Study

- SUPPORT was a randomized, multicenter trial of ventilation and oxygenation strategies in 24-27+6/7 week EGA infants; interventions began in the delivery room.
 - **SUPPORT results will be presented:**
 - May 1, 2:45 pm. Neonatal Medicine: Clinical Trials (Neil Finer)
 - May 2, 4:15 pm. Perinatal Epidemiology (Wally Carlo)



Methods: NEURO Study

- Prospective study of **early CUS** (4-14 days) and **late CUS** (35-42 weeks PMA) in a subcohort of SUPPORT
 - NEURO study also obtained **brain MRI** within 5 days of late CUS; analyses in progress
 - **Neurodevelopmental follow-up** will occur at 18-22 months and 6 ½ to 7 ½ years



Methods: Patients and Enrollment

- 16 Neonatal Research Network sites participated in NEURO secondary
- Sites implemented secondary enrollment strategy best suited for their center
 - Consent with or after main trial consent
- NEURO launched after the main trial started
 - IRB processes, neuroradiology arrangements for MRI portion of this study



Methods: Imaging and Local Reading

- NEURO protocol called for two CUS:
 - **Early:** 4-14 days of age
 - **Late:** 35-42 weeks PMA
- CUS views and planes obtained per local site clinical protocol; local readings per local clinical approach
- Trained research personnel at each site collected data from local radiologists' reports to NEURO study form



Methods: Central Reading

- Sites sent copies of early and late CUS to RTI International (NRN data center)
- Two masked central readers interpreted CUS during two 2-day reading sessions
- Central reader form collected detailed, hemisphere-specific radiologic observations and diagnostic data
 - Hintz SR, et. al. *J Pediatr* 2007;150:592



Methods: Analysis

- Reliability analysis by kappa statistic
 - Kappa = $\frac{\% \text{ observed agreement} - \% \text{ expected by chance}}{100\% - \% \text{ expected by chance}}$
 - ≥ 0.75 considered “substantial” to “excellent”
- Accuracy analysis by sensitivity and specificity
 - Each central reader as “gold standard” against which local reader was compared

Fleiss JL, Statistical Methods, 1981; Landis JR, Biometrics, 1977



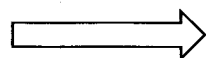
Results: Cohort and CUS scans

- **572 infants with early and late CUS**
- Early CUS obtained at $8_{\pm}4$ days of age
 - Median: 7 days
- Late CUS obtained at $37_{\pm}2$ weeks PMA
 - Median: 37 weeks PMA



Baseline Characteristics

N	572
BW, mean (SD)	848 (190) grams
EGA, mean (SD)	25.9 (1) weeks
Multiple gestation	23%
Male	56%
Race	
Non-Hispanic Black	30%
Non-Hispanic White	43%
Male	56%
Antenatal steroids	95%
Cesarean section	69%
Apgar score <3 at 5 minutes	3%
Maternal education < HS	21%



Central reader findings: **Early CUS**

	Central Reader 1	Central reader 2
EARLY CUS findings		
	N=572	N=572
Normal	72.0%	71.7%
Normal or choroid plexus bleed/cyst only	74.6%	72.6%
Any GMH or IVH	19.6%	20.8%
Grade 1 or 2	14.2%	12.2%
Grade 3 or 4	6.8%	9.6%
Moderate-severe ventricular enlargement	4.6%	4.6%
PVL (echodense or echolucent)	1.1%	0.5%
Cerebellar/posterior fossa lesion	1.6%	1.2%



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Central reader findings: Late CUS

	Central Reader 1	Central Reader 2
LATE CUS findings		
	N=571	N=572
Normal	70.8%	70.6%
Normal or choroid plexus bleed/cyst only	75.0%	73.1%
Any ventricular enlargement	7.7%	8.4%
Moderate-severe ventricular enlargement	4.4%	4.2%
Echolucent PVL (cPVL)	1.6%	1.1%
Porencephalic cyst (P-cyst)	2.1%	2.6%
cPVL or P-cyst or any ventriculomegaly or shunt	9.1%	9.6%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	6.5%	6.6%
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cPVL or P-cyst or any ventriculomegaly or shunt	9.1%	9.6%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	6.5%	6.6%
Cerebellar/posterior fossa	1.1%	0.4%



Central Reader Reliability: Early CUS

	Kappa	95% CI	PPA
EARLY CUS			
Normal vs. abnormal	0.76	(0.70, 0.82)	93%
Any GMH or IVH	0.79	(0.73, 0.85)	81%
Grade 1 or 2	0.52	(0.43, 0.61)	56%
Grade 3 or 4	0.77	(0.67, 0.87)	74%
Grade 3 or 4 or cPVL	0.75	(0.65, 0.85)	73%
Moderate-severe ventricular enlargement	0.84	(0.73, 0.95)	85%
PVL (echodense or echolucent)	0.22	(-0.15, 0.58)	22%



Central Reader Reliability: Late CUS

	Kappa	95% CI	PPA
LATE CUS			
Normal vs. abnormal	0.66	(0.59, 0.73)	90%
ANY ventricular enlargement	0.88	(0.83, 0.94)	89%
Moderate-severe ventricular enlargement	0.90	(0.84, 0.97)	91%
Echolucent PVL (cPVL)	0.45	(0.19, 0.71)	46%
Porencephalic cyst (P-cyst)	0.76	(0.58, 0.93)	76%
cPVL or P-cyst or any ventriculomegaly or shunt	0.84	(0.79, 0.90)	86%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	0.88	(0.82, 0.94)	89%



Accuracy of Local Interpretation Early CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any PVL	33.3%	98.2%	0%	97.9%



Accuracy of Local Interpretation Early CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any PVL	33.3%	98.2%	0%	97.9%



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	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any PVL	33.3%	98.2%	0%	97.9%



Accuracy of Local Interpretation Late CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
Any ventricular enlargement	77.3%	96.2%	75.0%	96.5%
Cystic PVL (cPVL)	66.7%	98.4%	50.0%	97.9%
Porencephalic cyst (P-cyst)	50.0%	99.6%	33.3%	99.5%
cPVL or P-cyst or any ventriculomegaly or shunt	80.8%	95.0%	74.5%	94.7%



Accuracy of Local Interpretation Late CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
Any ventricular enlargement	77.3%	96.2%	75.0%	96.5%
Cystic PVL (cPVL)	66.7%	98.4%	50.0%	97.9%
Porencephalic cyst (P-cyst)	50.0%	99.6%	33.3%	99.5%
cPVL or P-cyst or any ventriculomegaly or shunt	80.8%	95.0%	74.5%	94.7%



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	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
Any ventricular enlargement	77.3%	96.2%	75.0%	96.5%
Cystic PVL (cPVL)	66.7%	98.4%	50.0%	97.9%
Porencephalic cyst (P-cyst)	50.0%	99.6%	33.3%	99.5%
cPVL or P-cyst or any ventriculomegaly or shunt	80.8%	95.0%	74.5%	94.7%



Summary

- In the NICHD Neonatal Research Network NEURO CUS cohort:
 - Rates of major adverse findings on early and late CUS were low
 - Central reader reliability and local reader accuracy were very good for major adverse or composite CUS findings
 - Poorer for normal late CUS and rare findings, poorer reliability for lower grade hemorrhage



Limitations

- The protocol did not require local radiologist training or specific CUS views.
- Only two study scans were obtained.
- Unique cohort, part of a multicenter trial; results may not be generalizable.
 - Despite limitations, NEURO will be the largest extremely preterm cohort to date with CUS, brain MRI, and long-term follow-up - likely not possible outside of a multicenter network.



Discussion

- CUS were normal in ~70% of this cohort
 - But this does not assure normal outcome
 - O'Shea TM, et. al. *Pediatrics* 2008; Broitman E, et. al. *J Pediatr* 2007; Laptok A, et. al. *Pediatrics* 2005
 - Brain MRI results may augment CUS findings
- NEURO study will assess value of CUS and MRI, alone and with other risk factors, to predict neurologic and cognitive outcomes in early and later childhood

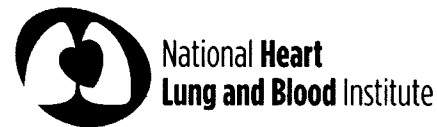


NICHD Neonatal Research Network Centers

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- RTI International
- Stanford University
- Tufts Medical Center
- University of Alabama – Birmingham
- University of California – San Diego
- University of Iowa
- University of New Mexico
- University of Rochester
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- University of Utah
- Wayne State University



NICHD

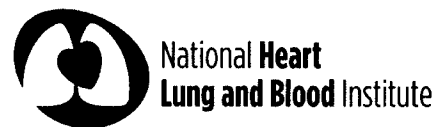


NICHD Neonatal Research Network

- **Special thanks to**
 - Neonatal Research Network site Coordinators
 - Meg Cunningham
 - Kris Zaterka
 - Carolyn Petrie-Huitema
 - Amanda Irene
 - Julie Croxford



NICHD



Higgins, Rosemary (NIH/NICHD) [E]

From: Michael O`Shea <moshea@wfubmc.edu>
Sent: Wednesday, March 24, 2010 10:13 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Rose,

Information for Wake Forest is correct

Thank you

Mike

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; Michael O`Shea; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

Hi ALL-

Attached are the two SUPPORT paper mastheads for authorship and the boilerplates. **I request that the site PI's please look at this and tell me by Thursday, March 25 if any additional changes are warranted.**

Also, Dr. Carlo has been contacted by NEJM and his paper has been selected to have an accompanying CME activity.

We do not as yet have a target publication date.

Thanks for all your help

Rose

Higgins, Rosemary (NIH/NICHD) [E]

From: Stenson, Ben <Ben.Stenson@luht.scot.nhs.uk>
Sent: Friday, May 21, 2010 9:10 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support

Thanks. That is very helpful.
Ben

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: 21 May 2010 13:57
To: Stenson, Ben
Subject: RE: Support

Ben

Discharge was defined as discharge home, transfer, or still hospitalized at one year. For transferred infants, we also used any subsequent information we had about whether the infant was later discharged home or died at the receiving hospital.

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Stenson, Ben [mailto:Ben.Stenson@luht.scot.nhs.uk]
Sent: Wednesday, May 19, 2010 3:16 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support

Thanks Rose

The primary outcome is death or Rop before discharge and death is given separately. My understanding is that this was death before discharge but I can't find a definition for discharge anywhere in the paper. Is this discharge to home or discharge out of the neonatal unit - ie could a child who got transferred on to picu or to gi because of short gut be classified as a discharge. Is there an age when still remaining in hospital somewhere was assumed to equal discharge alive?

Ben

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: 19 May 2010 19:44
To: Stenson, Ben
Subject: RE: Support

Ben

Can you direct to the exact table and line or statement in the manuscript?

I want to give you the correct information.

Best regards
Rose

-----Original Message-----

From: Stenson, Ben [mailto:Ben.Stenson@luht.scot.nhs.uk]
Sent: Wednesday, May 19, 2010 1:00 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support

Dear Rose

We are trying to work out what info to look at within our trial to compare our outcomes with support. Can you tell me how you defined discharge for the oxygen comparison.

Thanks

Ben Stenson

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mgantz@rti.org"
Cc: "adas@rti.org"; "nfiner@ucsd.edu"
Subject: Fw: Support
Date: Friday, May 21, 2010 7:30:00 AM

Marie - can you write exactly how we did this?
Thanks
Rose

----- Original Message -----

From: Stenson, Ben <Ben.Stenson@luht.scot.nhs.uk>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wed May 19 15:16:19 2010
Subject: RE: Support

Thanks Rose

The primary outcome is death or Rop before discharge and death is given separately. My understanding is that this was death before discharge but I can't find a definition for discharge anywhere in the paper. Is this discharge to home or discharge out of the neonatal unit - ie could a child who got transferred on to picu or to gi because of short gut be classified as a discharge. Is there an age when still remaining in hospital somewhere was assumed to equal discharge alive?

Ben

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: 19 May 2010 19:44
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Subject: RE: Support

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From: Stenson, Ben [<mailto:Ben.Stenson@luht.scot.nhs.uk>]
Sent: Wednesday, May 19, 2010 1:00 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support

Dear Rose

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Thanks

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From: [Susan Hintz](#)
To: [Meg Cunningham](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: a few slides for SUPPORT NEURO update
Date: Thursday, May 20, 2010 11:47:51 PM
Attachments: [NEURO update NRN SC meeting May 2010.pptx](#)

Hi all,

Here a just a few slides to update the Steering Committee for the SUPPORT NEURO secondary.

Rose, let me know if you think I am missing anything. I will be up very early in the morning anyway, so feel free to call me or email.

Thanks

Susan

SUPPORT NEURO Update

May 21, 2010 NRN Steering
Committee Meeting

NEURO Imaging update

- CUS reading and analysis:
 - NEURO cohort findings, reliability and accuracy analysis presented at Late Breaker PAS 2010
 - Manuscript in preparation
- MRI reading and analysis:
 - 558 MRIs expected
 - 502: central reader data keyed
 - 23: completed readings, sending to RTI to be keyed
 - 26: sites recently re-sent previously unreadable copies; currently with central reader

SUPPORT NEURO: Follow-up

- 18-22 month follow-up
 - Follow-up rates >90%, consistent with overall SUPPORT follow-up
 - Final window closes 4/30/2011
- 3-4 year tracking
 - Tracking status form (SEF01) completion rate per March 31 monthly report: **91.1%**
 - Only 9 SUPPORT NEURO patients thus far reported as “Lost to follow-up”

SUPPORT NEURO: Follow-up

- 6 ½ to 7 ½ year follow-up
 - Forms development has begun; goal for forms and MOP completion by winter 2010-11
 - Spanish speaking patients
 - **16.5% identify Spanish as primary language at 18-22 mo visit** among SUPPORT NEURO patients seen so far –
 - Range for sites: 0%-50%. Breakdown by site discussed at Follow-up PI meeting (PAS), also sent to sites
 - Spanish Gold Standard psychologists identified (Jean Lowe, Maria Elena DeAnda)

SUPPORT NEURO: Follow-up

- 6 ½ to 7 ½ year follow-up
 - Movement ABC II
 - Gold Standard training with Dr. David Sugden planned for mid-September
 - DVD will be created by these examiners for distribution to sites to assist in training
 - Planning for training for 6 ½ - 7 ½ year visit battery
 - Plan for follow-up visit training in **early Spring 2012**
 - Only 10 patients have windows that open before September 2012.
 - **6 ½ to 7 ½ year window for final NEURO enrollee closes in August 2016**

From: Webb, Robin E.
To: Webb, Robin E.; alaptook@WIHRI.org; Bradley Yoder; Das, Abhik; Gantz, Marie; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy.newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wallace, Dennis; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; Starlett Williams
Subject: RE: SUPPORT data queries
Date: Wednesday, May 19, 2010 2:25:17 PM

We're having difficulty coming up with a time for this call. Please let me know if you're available for the days/times below.

Thanks,
Robin

6/7 8:30-noon ET
6/8 8:30 – noon ET

From: Webb, Robin E.
Sent: Wednesday, May 12, 2010 7:26 PM
To: Abbot Laptook (alaptook@WIHRI.org); Bradley Yoder; Das, Abhik (adas@rti.org); Gantz, Marie (mgantz@rti.org); 'Higgins, Rosemary (NIH/NICHD) [E]'; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy.newman; 'nfiner@ucsd.edu'; Roger.Faix@hsc.utah.edu; Wallace, Dennis; Wally Carlo, M.D.; 'wrich@ucsd.edu'
Cc: (sharon.gough@hsc.utah.edu); 'Archer, Stephanie (NIH/NICHD) [E]'; 'Brenda Vecchio'; Cunningham, Meg; 'fmartinez@ucsd.edu'; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; Starlett Williams; Webb, Robin E.
Subject: SUPPORT data queries

We need to schedule a call to discuss the attached. Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin Webb
RTI, International
6110 Executive Blvd, Suite 902
Rockville, MD 20852

Mon 5/24
Wed 5/26
Thurs 5/27

Tues 6/1
Wed 6/2

Wed 6/9
Thurs 6/10
Fri 6/11

Mon 6/14
Tues 6/15
Wed 6/16
Thurs 6/17
Fri 6/18

Mon 6/21
Tues 6/22
Wed 6/23
Thurs 6/24
Fri 6/25

Mon 6/28
Tues 6/29
Wed 6/30
Thurs 7/1
Fri 7/2

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: Protocol tracker
Date: Wednesday, May 19, 2010 1:25:00 PM

They wanted \$170,000 so it went to protocol review and should be on the protocol tracker.

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, May 19, 2010 11:11 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Protocol tracker

I thought that the SUPPORT Oximetry proposal was a secondary Analysis, not protocol, right? So it would go to the PAS Abstract committee, not to the Protocol Subcommittee (and thus on the tracker), correct?

From: Poindexter, Brenda B [mailto:bpoindex@iupui.edu]
Sent: Wednesday, May 19, 2010 10:42 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: Protocol tracker

Stephanie,
I'll be in the office later this afternoon and can double check - the only one I didn't see was the support oximetry secondary that we reviewed a few weeks ago.
Brenda

Sent from my iPhone

On May 19, 2010, at 9:51 AM, "Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov> wrote:

Brenda,

Do you have any changes to make to the tracker? We need to print these up today for the meeting.

Thanks,

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 17, 2010 12:59 PM

To: Brenda Poindexter (bpoindex@iupui.edu)
Cc: Richard Ehrenkranz (richard.ehrenkranz@yale.edu)
Subject: Protocol tracker

Hi Brenda,

Attached is the latest version of the Protocol Tracker. I've gone back through my emails/calendar and entered in any protocol calls that I could find. Please let me know if I am missing any, or if anyone has sent in revisions/new protocols that are not on the tracker.

I will print handouts for the meeting.

Stephanie

Higgins, Rosemary (NIH/NICHD) [E]

From: Stenson, Ben <Ben.Stenson@luht.scot.nhs.uk>
Sent: Wednesday, May 19, 2010 1:00 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Support

Dear Rose

We are trying to work out what info to look at within our trial to compare our outcomes with support. Can you tell me how you defined discharge for the oxygen comparison.

Thanks

Ben Stenson

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Webb, Robin E."
Subject: RE: SUPPORT CALL
Date: Wednesday, May 19, 2010 9:46:00 AM

Can we try the following times for
6/7 8:30-noon ET
6/8- 8:30 – noon ET

Sorry for the trouble.

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, May 19, 2010 9:28 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT CALL

Tuesday, 6/1 between 12-3pm works for Finer and Carlo but Walsh isn't available. Friday 6/11 Carlo and Walsh are available but not Finer. The days that I polled in between those dates at least two of the three needed are unavailable. I didn't get availability for 6/7 & 8 since I knew you were in New Mexico.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 19, 2010 8:52 AM
To: Webb, Robin E.
Subject: RE: SUPPORT CALL

We would like to do it sooner. Who has given you limited options or is it possible to do it while I am in New Mexico? (6/7 or 6/8 – is there a time on these two days that we can get the others?) Let me know

Thanks
Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, May 19, 2010 8:48 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT CALL

Monday, 6/21 is the only day that works for everyone listed below. Is that too late?

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 19, 2010 8:36 AM
To: Webb, Robin E.
Subject: RE: SUPPORT CALL

At least NEIL, Wally, Michele, me + Abhik

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, May 19, 2010 8:35 AM
To: Higgins, Rosemary (NIH/NICHD) [E]

Subject: RE: SUPPORT CALL

Who needs to be on this call?

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 19, 2010 8:32 AM
To: Webb, Robin E.
Subject: RE: SUPPORT CALL

Yes and to prioritize all of the secondary studies

Thanks
Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, May 19, 2010 8:31 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT CALL

Hi Rose,

I had sent out an email polling for availability to discuss two secondary data analysis proposals for SUPPORT,,,,one looking at the DR CPAP portion of the study, the other at the oxygen sat target portion. Is that what this call is for? Or do you need another one?

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, May 18, 2010 12:33 PM
To: Webb, Robin E.
Subject: SUPPORT CALL

Robin

Can you set up a SUPPORT call ASAP to discuss the SUPPORT secondary studies?

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Wally Carlo, M.D."; "Neil Finer"
Subject: RE: SUPPORT papers
Date: Wednesday, May 19, 2010 9:08:00 AM

Wally –

I think because they are an early release, the authors and folks in the boilerplate don't show up yet. Once the paper is "published" I am hoping this will change.

Rose

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Wednesday, May 19, 2010 9:06 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Neil Finer
Subject: SUPPORT papers

Dear Rose and Neil:

I look for the papers in Pubmed and it was very hard to find them. I was disappointed it cannot be searched by authors. Maybe it will be archived by authors later.

Just wanted to give you the heads up.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Tuesday, May 18, 2010 11:41 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Martinez, Fernando
Subject: RE: THANKS TO THE COORDINATORS

That's fine
I'll be available
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center
402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Monday, May 17, 2010 2:59 PM
To: Finer, Neil
Subject: Re: THANKS TO THE COORDINATORS

I don't think so since we had a few calls - we need to have a call soon to organize the secondaries.
Can you join at 1105 ET (805 PT) on friday?

Thanks
Rose

----- Original Message -----

From: Finer, Neil <nfiner@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Mon May 17 18:00:39 2010
Subject: RE: THANKS TO THE COORDINATORS

Hi Rose
Is there a SUPPORT Subcommittee meeting at the NRN meeting this week?
I do not see it on the schedule
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology

Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center
402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]

Sent: Sunday, May 16, 2010 2:10 PM

To: Rich, Wade; Nancy Peters; Ruth Everett; Reubens, Linda; rbara@wayne.med.edu; (Karen.Osborne@hsc.utah.edu); Angelita Hensman; Becky bara; Bethany Ball; Brenda MacKinnon (bmackinnon@tuftsmedicalcenter.org); Cathy Grisby (cathy.grisby@uc.edu); Conra Backstrom; Diana Vasil; Diane Wilson; Donia Campbell; Elizabeth Billian; Ellen Hale; Georgia McDavid; Karen Johnson (karen-johnson@uiowa.edu); Kimberley Fisher; Leslie Wilson; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Sandra Grimes

Cc: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa

Subject: THANKS TO THE COORDINATORS

Importance: High

Hi

I would like to thank the coordinators for the awesome job with SUPPORT!!!

The manuscripts have been released on-line by the New England Journal of Medicine and will appear in the May 27 print issue.

I attached the files to the email - you can also access them at <http://content.nejm.org/> to see the on-line release of both papers concurrent with Drs. Finer and Carlo's presentations early today at the American Thoracic Society meeting in New Orleans

THANKS FOR ALL THE HARD WORK!!!!!!!

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network Pregnancy and Perinatology Branch Center for Developmental Biology and Perinatal Medicine Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health 6100 Executive Blvd., Room 4B03 MSC 7510 Bethesda, MD 20892 For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "nfiner@ucsd.edu"
Subject: Re: THANKS TO THE COORDINATORS
Date: Monday, May 17, 2010 5:58:42 PM

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Telephone: 619-543-3759
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Sent: Sunday, May 16, 2010 2:10 PM
To: Rich, Wade; Nancy Peters; Ruth Everett; Reubens, Linda; rbara@wayne.med.edu; (Karen.Osborne@hsc.utah.edu); Angelita Hensman; Becky bara; Bethany Ball; Brenda MacKinnon (bmackinnon@tuftsmedicalcenter.org); Cathy Grisby (cathy.grisby@uc.edu); Conra Backstrom; Diana Vasil; Diane Wilson; Donia Campbell; Elizabeth Billian; Ellen Hale; Georgia McDavid; Karen Johnson (karen-johnson@uiowa.edu); Kimberley Fisher; Leslie Wilson; Monica Collins; monica.konstantino@yale.edu; Nancy Miller; Nancy Newman; Sandra Grimes
Cc: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Subject: THANKS TO THE COORDINATORS
Importance: High

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THANKS FOR ALL THE HARD WORK!!!!!!!

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network Pregnancy and Perinatology Branch Center for Developmental Biology and Perinatal Medicine Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health 6100 Executive Blvd., Room 4B03 MSC 7510 Bethesda, MD 20892 For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Raju, Tonse (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/NICHD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
Subject: SUPPORT PAPER: Mean Airway Pressure--not Mean Arterial Pressure
Date: Monday, May 17, 2010 4:00:55 PM
Attachments: image003.png

Hi Rose/Stephanie:

Minor typos—NOT A BIG DEAL: On page 3 of the CPAP paper, 2nd column, 1st paragraph of the "Surfactant Group" in methods, twice you meant to say "mean airway pressure" instead of "mean arterial pressure". See below.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a PaCO₂ of less than 50 mm Hg and a pH higher than 7.30, an FiO₂ of 0.35 or less with an SpO₂ of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

That said, this is a tough, and well done study; there will be more time for journal club discussions, dissection and understanding! But, congrats in order.

Tonse N.K. Raju, MD, DCH
PPB/NIH
Phone: 301-402-1872

-----Original Message-----

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 17, 2010 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/OD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
Subject: NRN in the New England Journal of Medicine

FYI, the two NRN papers were e-published this weekend. Wohoo!

Stephanie Wilson Archer

The Eunice Kennedy Shriver

National Institute of Child Health and Human Development

Pregnancy & Perinatology Branch

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Rockville, MD 20852

Tel. 301-496-0430

Fax 301-496-3790

archerst@mail.nih.gov <mailto:archerst@mail.nih.gov>

From: NEJM [mailto:nejmtoc@nejm.org]

Sent: Sunday, May 16, 2010 1:54 PM

To: Archer, Stephanie (NIH/NICHD) [E]

Subject: May 16, 2010 -- Online First from the New England Journal of Medicine

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Medicine<http://nejm.org/earlyrelease/Early_etoc/nejm_1line.gif>

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q=137%3B67397896%3BPeamGMYSJ3WhBMuyLpPJsakcqLZx8yD3pWRGku1wnKw%3D> on May 16,

2010.

<http://nejm.org/earlyrelease/Early_etoc/grey_dot_rule462.jpg>

Original Article

Target Ranges of Oxygen Saturation in Extremely Preterm Infants <<http://click2.nejm.org/cts/click?q=137%3B67397896%3BPeamGMYSJ3WhBMuyLpPJsXG0keAP9f1tpWRGku1wnKw%3D>>
SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network

Original Article

Early CPAP versus Surfactant in Extremely Preterm Infants <<http://click2.nejm.org/cts/click?q=137%3B67397896%3BPeamGMYSJ3WhBMuyLpPJsXNm kudn5OzQpWRGku1wnKw%3D>>
SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network

Editorial

CPAP and Low Oxygen Saturation for Very Preterm Babies? <<http://click2.nejm.org/cts/click?q=137%3B67397896%3BPeamGMYSJ3WhBMuyLpPJsSmXoVFASZRDpWRGku1wnKw%3D>>
C.J. Morley

<http://nejm.org/earlyrelease/Early_etoc/grey_dot_rule462.jpg>

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<http://nejm.org/earlyrelease/Early_etoc/grey_dot_rule462.jpg>

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<<http://click2.nejm.org/cts/click?q=137%3B67397896%3BFES6rnuVO610mB7iS5KwHg%3D%3D>>

SURFACTANT GROUP

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From: Willinger, Marian (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/NICHD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]
Subject: RE: NRN in the New England Journal of Medicine
Date: Monday, May 17, 2010 11:07:48 AM

Congratulations Rose and Stephanie- this is great! It was tough study.

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 17, 2010 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/OD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
Subject: NRN in the New England Journal of Medicine

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Stephanie Wilson Archer
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Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

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Sent: Sunday, May 16, 2010 1:54 PM
To: Archer, Stephanie (NIH/NICHD) [E]
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Target Ranges of Oxygen Saturation in Extremely Preterm Infants

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CPAP and Low Oxygen Saturation for Very Preterm Babies?

C.J. Morley

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From: Tolivaisa, Susan (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: NRN in the New England Journal of Medicine
Date: Monday, May 17, 2010 10:39:18 AM

Congrats!!

Best - Susan

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 17, 2010 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/OD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
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National Institute of Child Health and Human Development
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From: Spong, Catherine (NIH/NICHD) [E]
To: Ilekis, John (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/NICHD) [E]; Signore, Caroline (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
Subject: Re: NRN in the New England Journal of Medicine
Date: Monday, May 17, 2010 10:32:02 AM

Wahooooo!!!
Catherine Y Spong MD
Chief, Pregnancy and Perinatology Branch
Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH
6100 Executive Blvd
Bethesda MD 20892 (express mail Rockville MD 20852)
Phone 301 435 6894
Fax 301 496 3790
Email. Spongcc@mail.nih.gov

From: Ilekis, John (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/OD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
Sent: Mon May 17 10:30:14 2010
Subject: RE: NRN in the New England Journal of Medicine

Congrats to Rose and Stephanie!

John

John V. Ilekis, PhD
Health Scientist Administrator,
Program Scientist, Genomic & Proteomic Network for Preterm Birth Research,
National Institutes of Health,
Eunice Kennedy Shriver National Institute of Child Health and Human Development,
Center for Developmental Biology and Perinatal Medicine,
Pregnancy and Perinatology Branch,
Room 4B03C, 6100 Executive Blvd.
Rockville, MD 20852

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From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Monday, May 17, 2010 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Ilekis, John (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Raju, Tonse (NIH/NICHD) [E]; Reddy, Uma (NIH/NICHD) [E]; Rogers, Christine (NIH/OD) [E]; Signore, Caroline (NIH/NICHD) [E]; Spong, Catherine (NIH/NICHD) [E]; Tolivaisa, Susan (NIH/NICHD) [E]; Willinger, Marian (NIH/NICHD) [E]
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From: [Wilson, Leslie Dawn](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: THANKS TO THE COORDINATORS
Date: Sunday, May 16, 2010 8:37:11 PM

Thank you-- I appreciate your leadership and also thoughtfulness to include us.

Leslie Wilson, BSN, CCRC
Research Manager
699 West Drive, RR 208
Indianapolis, IN 46202
Ph: 317.274.8255
Fax: 317.278.7856
Pager: 317.312.1121
E-mail: ldw@iupui.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Sunday, May 16, 2010 5:09 PM
To: Rich, Wade; Nancy Peters; Ruth Everett; Reubens, Linda; rbara@wayne.med.edu;
(Karen.Osborne@hsc.utah.edu); Angelita Hensman; Becky bara; Bethany Ball; Brenda MacKinnon
(bmackinnon@tuftsmedicalcenter.org); Cathy Grisby (cathy.grisby@uc.edu); Conra Backstrom; Diana Vasil;
Herron, Dianne E; Donia Campbell; Elizabeth Billian; Ellen Hale; Georgia McDavid; Karen Johnson (karen-johnson@uiowa.edu); Kimberley Fisher; Wilson, Leslie Dawn; Monica Collins; monica.konstantino@yale.edu;
Nancy Miller; Nancy Newman; Sandra Grimes
Cc: finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema,
Carolyn Petrie; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das;
alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Poindexter, Brenda
B; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard
(E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler
(kurt.schibler@cchmc.org); Matthew Bizarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo
Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail);
Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Subject: THANKS TO THE COORDINATORS

Hi

I would like to thank the coordinators for the awesome job with SUPPORT!!!

The manuscripts have been released on-line by the New England Journal of Medicine and will appear in the May 27 print issue.

I attached the files to the email - you can also access them at <http://content.nejm.org/> to see the on-line release of both papers concurrent with Drs. finer and Carlo's presentations early today at the American Thoracic Society meeting in New Orleans

THANKS FOR ALL THE HARD WORK!!!!!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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higginsr@mail.nih.gov

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Saturday, May 15, 2010 6:29 PM
To: Susan Hintz; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wally Carlo M.D.
Subject: RE: ATS presentation

Thanks Susan
I hope things are OK for you and your family Be well Neil

-----Original Message-----

From: Susan Hintz [<mailto:rhintz@stanford.edu>]
Sent: Saturday, May 15, 2010 1:18 PM
To: higgins Higgins
Cc: Finer, Neil; Wally Carlo M.D.
Subject: ATS presentation

Hi all,

Just emailing you to wish you great success at the ATS SUPPORT presentation! I am sure it will be fantastic - wish I could be there to cheer you on in person!

Safe travels,

Susan

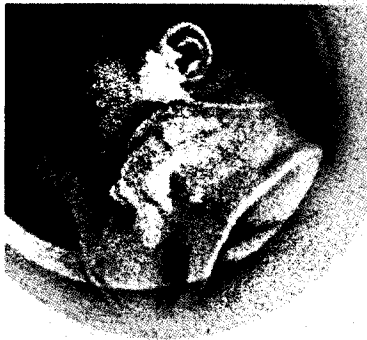
Sent from my iPhone

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Date: Saturday, May 15, 2010 10:30:00 AM
Attachments: [SUPPORT TRAIL OVERVIEW FOR ATS.ppt](#)

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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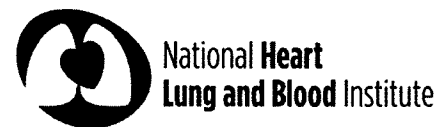
NICHD

Neonatal Research Network



SUPPORT TRIAL

NICHD Neonatal Research Network



NICHD NRN Mission

The Neonatal Research Network is designed to conduct studies to investigate the safety and efficacy of treatment and management strategies to care for newborn infants.



Origins of Neonatal Research Network (NRN)

- Neonatal management, especially for high-risk term and preterm infants, has often adopted practices without objective evaluation
- NICHD established the Neonatal Research Network in 1986 to address the need for well-designed clinical trials in Neonatal Medicine



NICHD NRN Aims

- Identify priority issues for research in the promotion of infant health and prevention of disease
- Evaluate interventions for efficacy, safety, and cost-effectiveness, including:
 - Translational research
 - Genetics
 - New technologies



Background NRN

- Collaborative participation on common protocols
- Cooperative agreements
- Competitively peer-reviewed
 - Open competition
 - Content of grant, concept proposal, depth of faculty and institution
 - Priority score
 - Diversity in population



Neonatal Practice 2003-2004

- Trend towards more use of CPAP
- Trend towards use of lower oxygen saturation targets

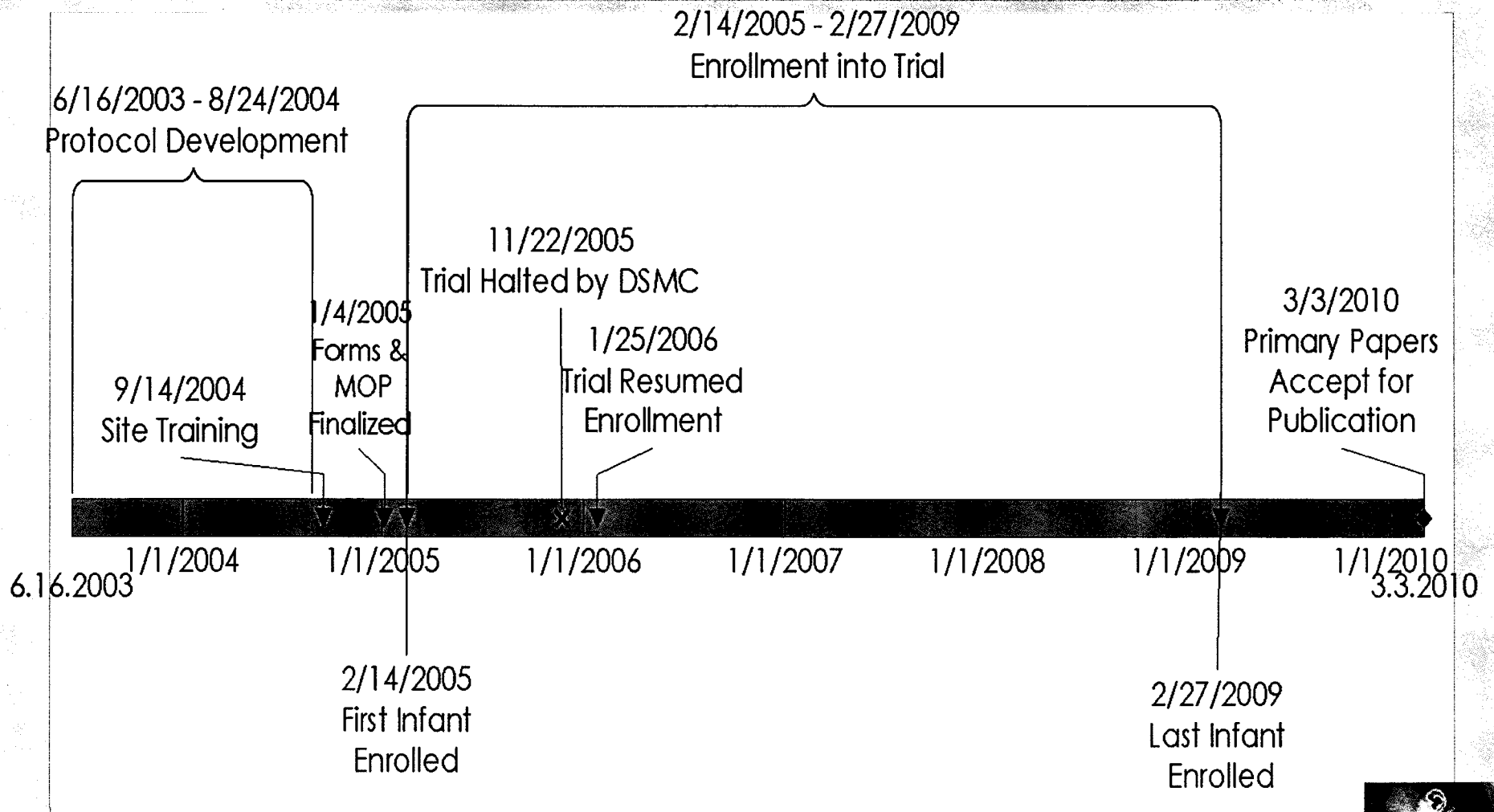


SUPPORT RESEARCH QUESTIONS

- Where do we target saturations for optimal outcome?
 - Low 90's
 - Mid-high 80's
- What's better?
 - Early Surfactant
 - CPAP

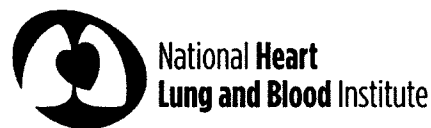


SUPPORT TIMELINE



NICHD Neonatal Research Network SUPPORT Trial Centers (2004-2009)

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- Research Triangle Institute
- Stanford University
- Tufts Medical Center
- University of Alabama – Birmingham
- University of Cincinnati
- University of California – San Diego
- University of Iowa
- University of Miami
- University of New Mexico
- University of Rochester
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- University of Utah
- Wayne State University
- Wake Forest University
- Yale University



NICHD



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Date: Friday, May 14, 2010 4:45:04 PM
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Hi

I would like to thank the coordinators for the awesome job with SUPPORT!!!

The manuscripts have been released on-line by the New England Journal of Medicine and will appear in the May 27 print issue.

I attached the files to the email - you can also access them at <http://content.nejm.org/> to see the on-line release of both papers concurrent with Drs. Finer and Carlo's presentations early today at the American Thoracic Society meeting in New Orleans

THANKS FOR ALL THE HARD WORK!!!!!!!

Rose

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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

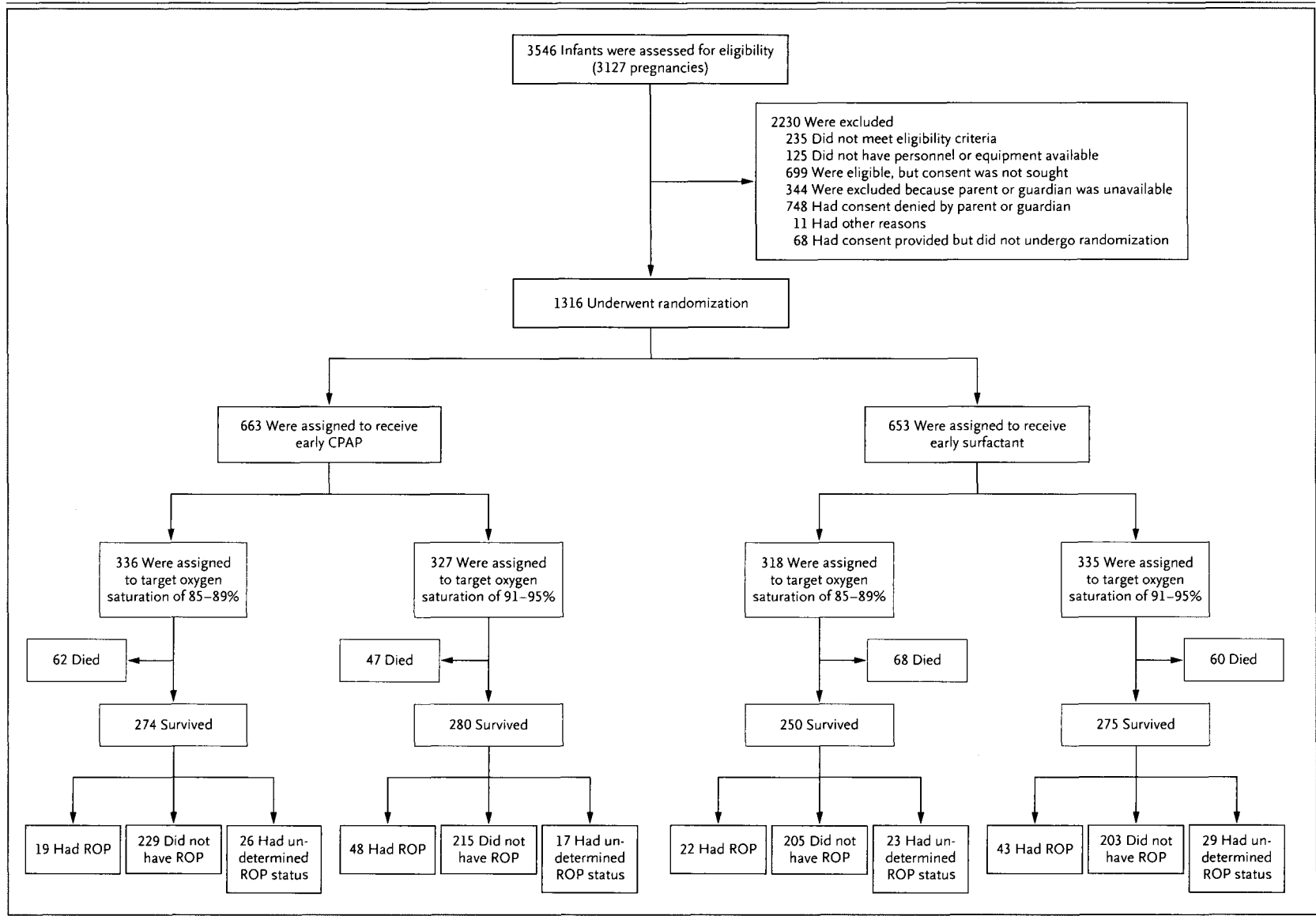


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)	Adjusted Relative Risk (95% CI)
	no./total no. (%)		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$; number needed to treat, 11). Although

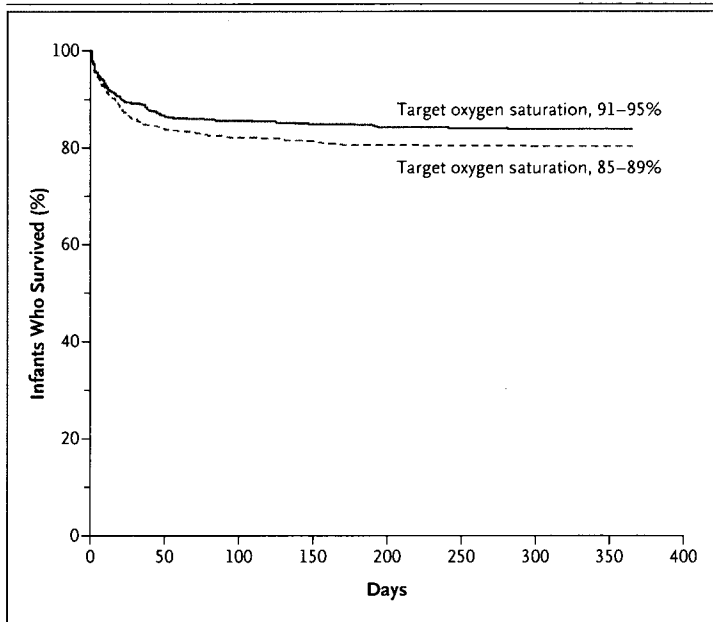


Figure 2. Kaplan–Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.
 Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

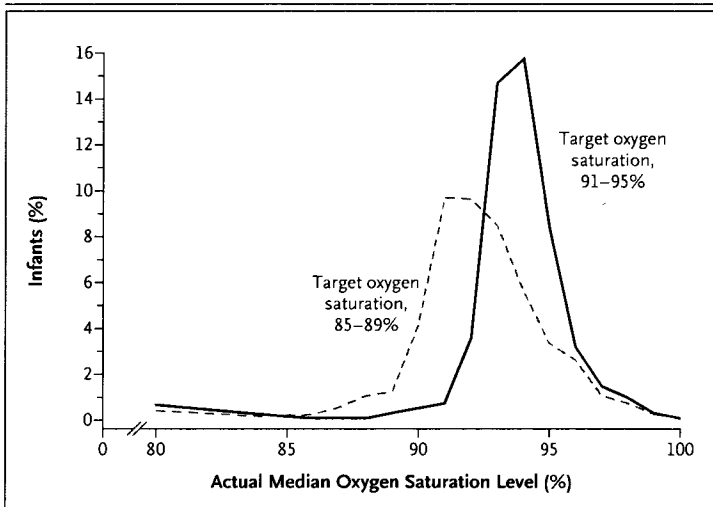


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.
 The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO₂ concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, U11 RR25008, U11 RR24139, U11 RR24979, and U11 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010. DOI: [10.1056/NEJMoa0911781](https://doi.org/10.1056/NEJMoa0911781).

Appendix Table 1: Cause of Death in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth

Weight Infants

Category – no./total no. (%)	Lower Saturation	Higher Saturation
	Group	Group
	n/N (%)	n/N (%)
Respiratory distress syndrome	31/130 (23.8)	31/107 (29.0)
Infection	25/130 (19.2)	21/107 (19.6)
Necrotizing enterocolitis	23/130 (17.7)	14/107 (13.1)
Bronchopulmonary dysplasia	14/130 (10.8)	10/107 (9.3)
Central nervous system insult	12/130 (9.2)	9/107 (8.4)
Immaturity	7/130 (5.4)	3/107 (2.8)
Other	18/130 (13.8)	19/107 (17.8)
Causes of death did not differ		

Appendix Table 2: Effect of Retinopathy Adjudication for Low vs. High Oxygen Saturation Target Groups

Characteristic	Lower Saturation	Higher Saturation	Relative Risk for	Adjusted
	Group (N=654)	Group (N=662)	Low SpO ₂ vs. High	P value
	n/N (%)	n/N (%)	SpO ₂ (95% CI)	
Severe retinopathy/death, All outcomes (non-adjudicated)	171/605 (28.3)	198/616 (32.1)	0.9 (0.76, 1.06)	0.205
Severe retinopathy among survivors, All outcomes (non-adjudicated)	41/475 (8.6)	91/509 (17.9)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed by majority rule*	171/642 (26.6)	198/656 (30.2)	0.91 (0.77, 1.07)	0.253
Severe retinopathy among survivors, Cases considered confirmed by majority rule*	41/512 (8.0)	91/549 (16.6)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed majority rule* when “unknown cases” considered to have severe retinopathy†	183/654 (28.0)	204/662 (30.8)	0.93 (0.79, 1.1)	0.412
Severe retinopathy among survivors, Cases confirmed by majority rule when “unknown cases” considered to have severe retinopathy†	53/524 (10.1)	97/555 (17.5)	0.62 (0.45, 0.84)	0.002

Relative risks are adjusted for gestational age stratification, center, and familial clustering:

*Majority rule: If two reviewers determined that the infant ‘Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye’ then retinopathy=N; If two reviewers determined that ‘There is no way to know if severe retinopathy criteria may have been met’ then severe retinopathy=missing.

†If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; if two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=Y.

Appendix Table 3. Other Outcomes in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth Weight Infants

Outcome	Lower Saturation Group	Higher Saturation Group	Adjusted P value [§]
Length of stay any hospital, (days) m±SE*	104.5 ± 2.0	106.4 ± 2.0	0.45
Length of stay at study hospital, (days) m±SE*	99.8 ± 2.0	103.0 ± 2.0	0.22
Duration of mechanical ventilation, (days) m±SE [†]	25.5 ± 1.1	26.9 ± 1.0	0.30
Duration of oxygen supplementation, (days) m±SE [†]	59.8 ± 1.6	67.4 ± 1.5	<0.001
Continuous positive airway pressure, (days) m±SE [†]	17.1 ± 0.6	17.0 ± 0.6	0.94
Nasal synchronized intermittent mandatory ventilation, (days) m±SE [†]	3.3 ± 0.3	3.8 ± 0.3	0.14
Alive off mechanical ventilation by day 14, (days) – no. (%)	332/644 (51.6)	326/655 (49.8)	0.86
Alive off mechanical ventilation by day 7, (days) – no. (%)	351/648 (54.2)	329/659 (49.9)	0.27
Percent of time in actual oxygen saturation range 84-96%, (%) m±SD‡	66.9 ± 13.9	68.0 ± 15.2	0.16¶

*Among survivors to discharge, transfer or one year; maximum value is 366 days

[†]Among survivors to discharge, transfer or 120 days; maximum value is 120 days

‡Percent of time based only on total time on oxygen supplementation

§Adjusted for stratification factors (study center, gestational age group) as well as for familial clustering

¶Unadjusted P value

ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P<0.001$), required fewer days of mechanical ventilation ($P=0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P=0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of members of the Writing Committee and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network are listed in the Appendix. Address reprint requests to Dr. Neil N. Finer at the University of California at San Diego, 402 Dickinson St., MPF 1-140, San Diego, CA 92103-8774, or at nfiner@ucsd.edu.

This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (FIO₂) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO₂) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide (PaCO₂) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a PaCO₂ below 65 mm Hg with a pH higher than 7.20, an SpO₂ above 88% with an FIO₂ below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a PaCO₂ of less than 50 mm Hg and a pH higher than 7.30, an FIO₂ of 0.35 or less with an SpO₂ of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

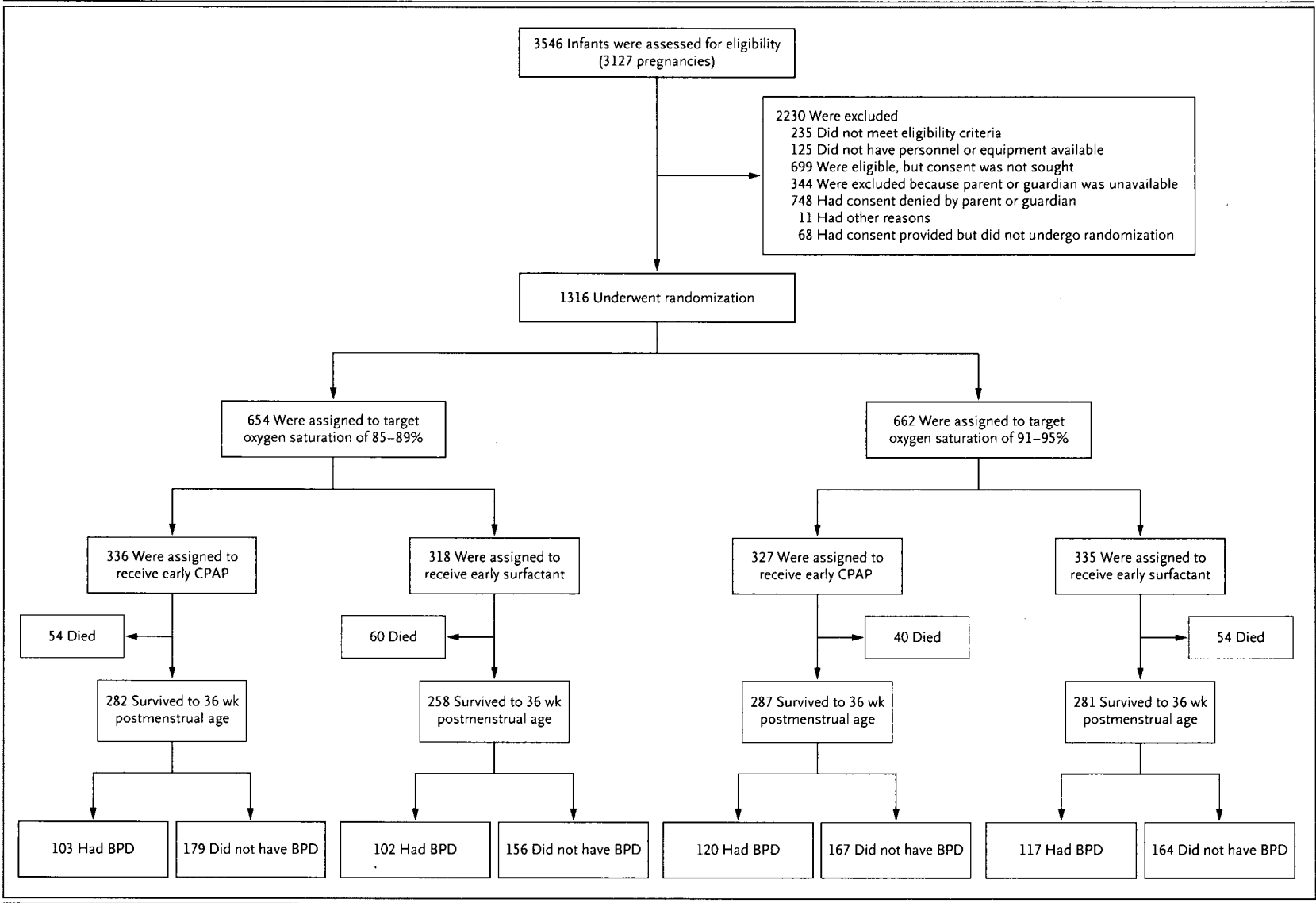


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Variable	CPAP (N = 663)	Surfactant (N = 653)	Relative Risk with CPAP (95% CI)	Adjusted P Value
	<i>no./total no. (%)</i>			
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N = 663)	Surfactant (N = 653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that

Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010. DOI: 10.1056/NEJMoa0911783.

Web Appendix Tables

Table A1. Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted	35.8 ± 1.5	38.7 ± 1.6	-3.0 (-7.2, 1.3)	0.17
Mean±StdErr, Unadjusted Median (IQR) (N=421)	29.5 (10, 48)	33 (14, 56)		
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

Table A2. Cause of Death for 24 to 25 week stratum

Contributory Cause of Death	CPAP (N=68)	Surfactant (N=90)
Respiratory distress syndrome	13/68 (19.1)	31/90 (34.4)
Bronchopulmonary dysplasia	10/68 (14.7)	7/90 (7.8)
Infection	14/68 (20.6)	15/90 (16.7)
Necrotizing enterocolitis	10/68 (14.7)	16/90 (17.8)
Central nervous center insult	11/68 (16.2)	5/90 (5.6)
Immaturity	3/68 (4.4)	5/90 (5.6)
Other	7/68 (10.3)	11/90 (12.2)

Table A3. Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P-value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the FiO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Kattwinkel, John *HS"
Subject: ****Confidential****
Date: Friday, May 14, 2010 2:39:00 PM
Attachments: Carlo.pdf
Finer.pdf
Morley.pdf
SUPPORT_Press release.docx

John

Here are the items discussed. As per our conversation, these need to be kept confidential until the embargo is lifted on Sunday May 16 at 1 PM ET.

Regards
Rose

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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

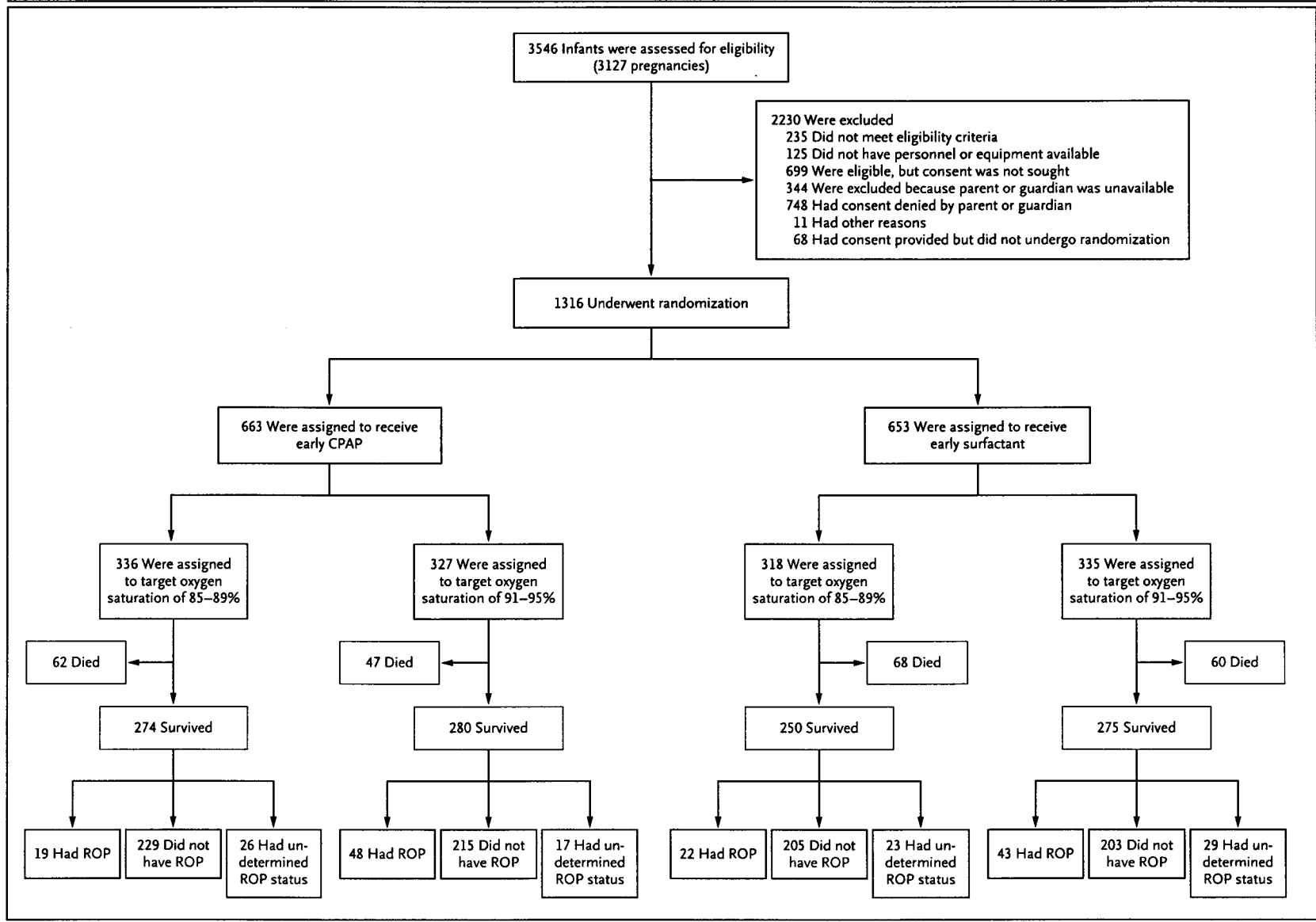


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; P<0.001; number needed to treat, 11). Although

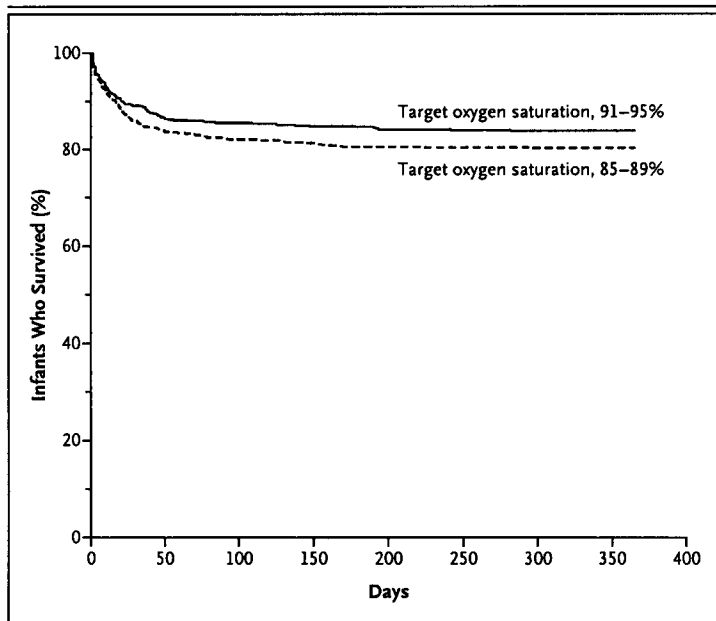


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.

Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

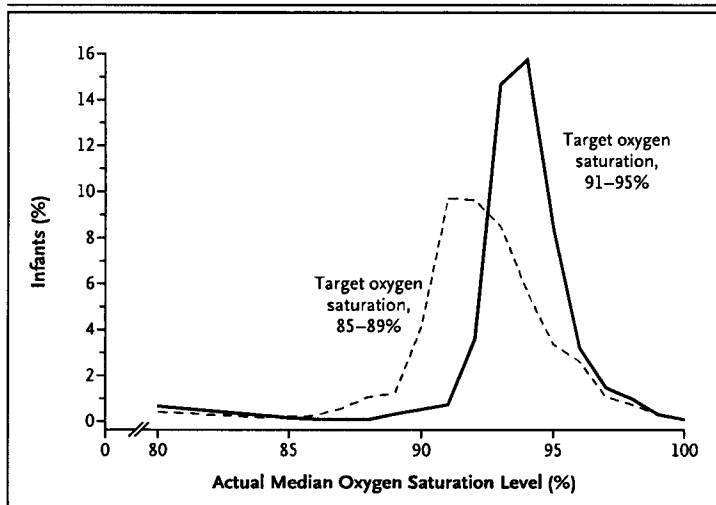


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.

The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO_2 concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P < 0.001$), required fewer days of mechanical ventilation ($P = 0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P = 0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (F_{iO_2}) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an F_{iO_2} below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an F_{iO_2} of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

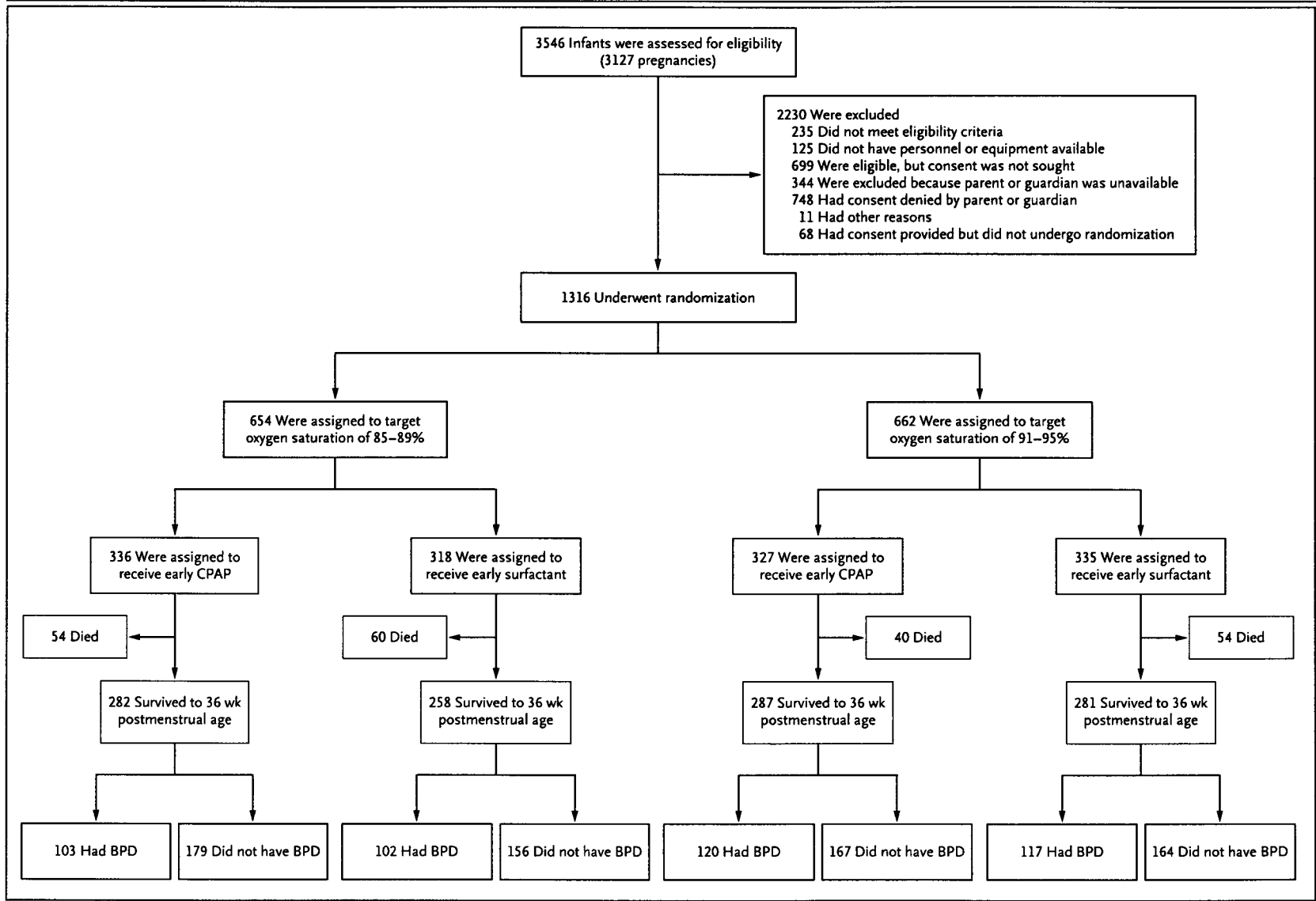


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Table 2. Apgar Scores of Newborns and Interventions in the Delivery Room and NICU.*				
Variable	CPAP (N = 663)	Surfactant (N = 653)	Relative Risk with CPAP (95% CI)	Adjusted P Value
	<i>no./total no. (%)</i>			
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO_2) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide ($PaCO_2$), pH, the fraction of inspired oxygen (FiO_2), and SpO_2 were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; $P=0.30$). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) ($P<0.001$ for both comparisons), and required ventilation for an average of 3 days less ($P=0.03$). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the FiO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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U.S. Department of Health and Human Services

NIH News

National Institutes of Health

Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
<http://www.nichd.nih.gov/>

Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition
Early CPAP as Effective For Premies as Ventilator, With Fewer Complications

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by The New England Journal of Medicine. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

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From: Higgins, Rosemary (NIH/NICHD) [E]
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Subject: ****Confidential****
Date: Friday, May 14, 2010 2:38:00 PM
Attachments: Carlo.pdf
Finer.pdf
Morley.pdf
SUPPORT Press.release.docx

LuAnn

Here are the items discussed. As per our conversation, these need to be kept confidential until the embargo is lifted on Sunday May 16 at 1 PM ET.

Regards
Rose

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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

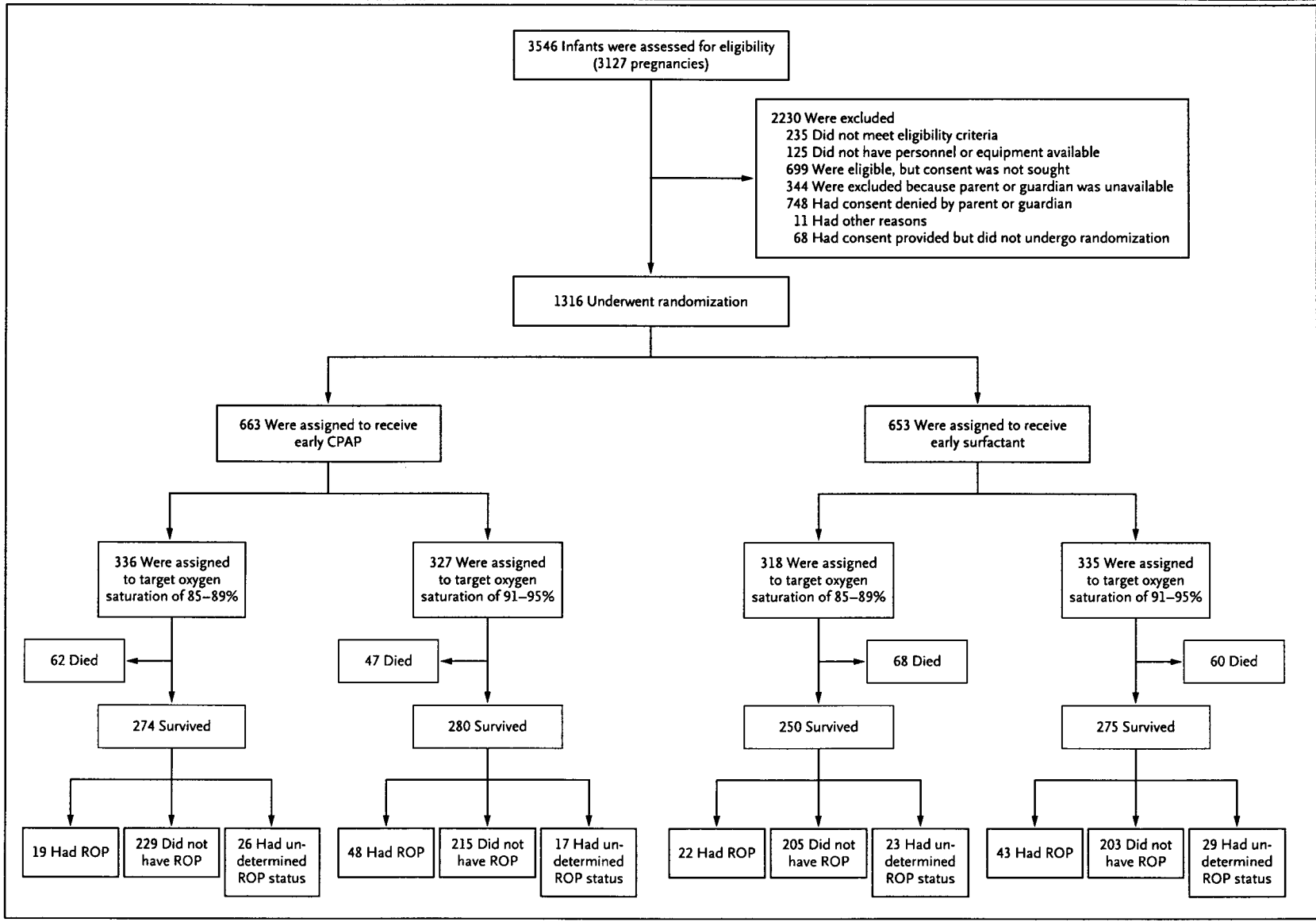


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. $P > 0.05$ for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P = 0.21$) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found ($P = 0.57$). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; $P = 0.04$; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; P<0.001; number needed to treat, 11). Although

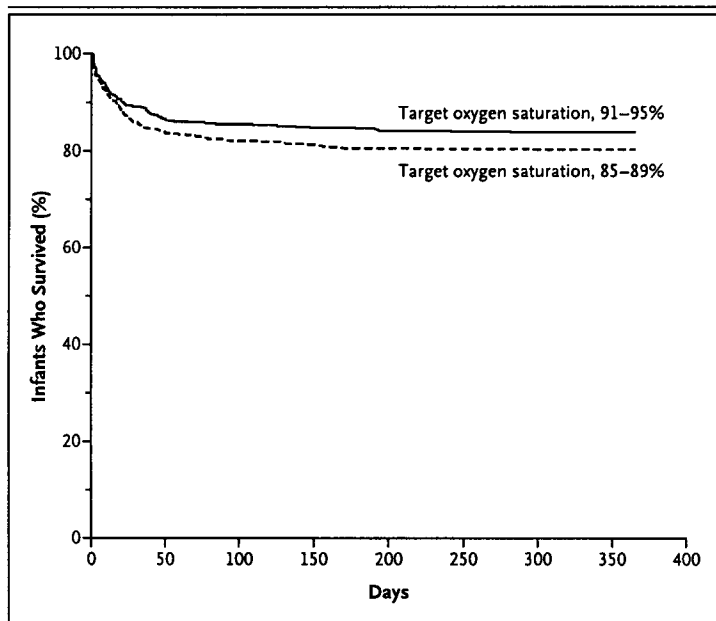


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.
Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

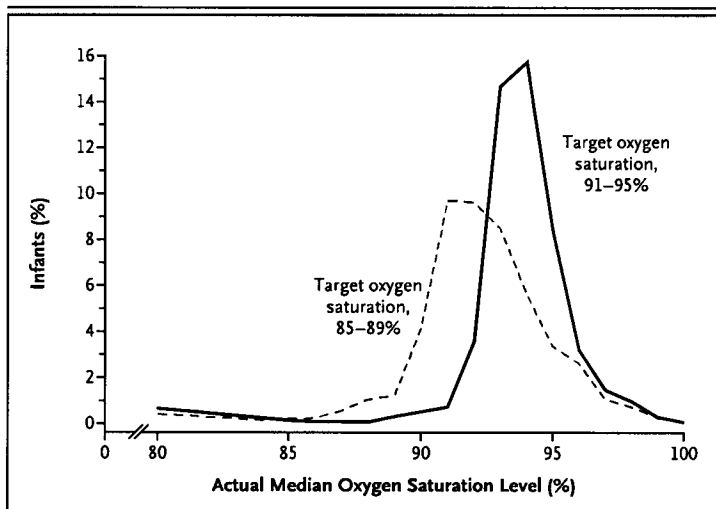


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.
The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the F_{iO_2} concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, U10 RR25008, U10 RR24139, U10 RR24979, and U10 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikarria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

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ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P < 0.001$), required fewer days of mechanical ventilation ($P = 0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P = 0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (F_{iO_2}) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an F_{iO_2} below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an F_{iO_2} of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes—four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

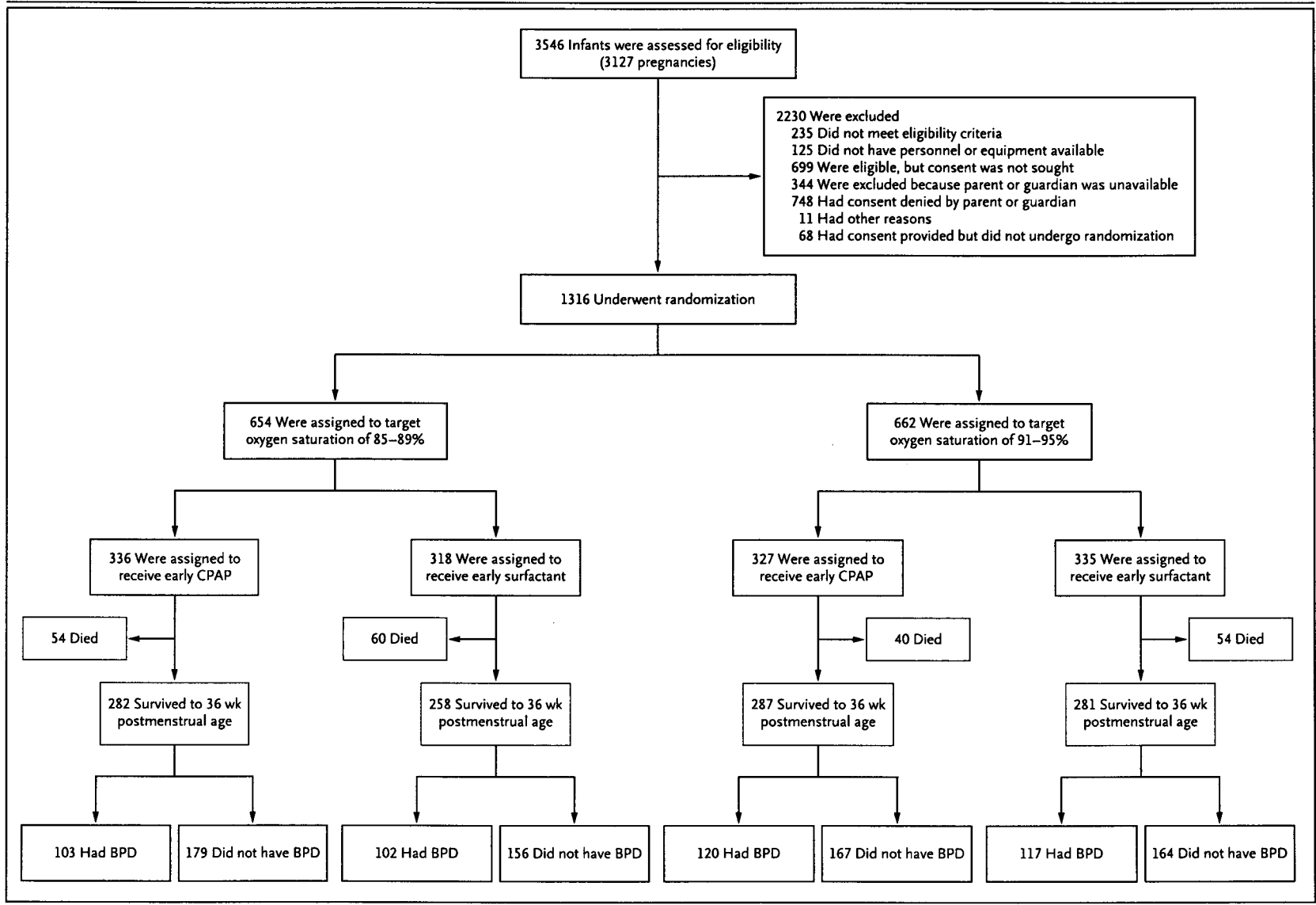


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Variable	CPAP (N=663) no./total no. (%)	Surfactant (N=653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that

Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the F_{iO_2} to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
<http://www.nichd.nih.gov/>

Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition
Early CPAP as Effective For Premies as Ventilator, With Fewer Complications

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by The New England Journal of Medicine. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

The National Institutes of Health (NIH) —The Nation’s Medical Research Agency— includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

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Here are the items discussed. As per our conversation, these need to be kept confidential until the embargo is lifted on Sunday May 16.

Regards
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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

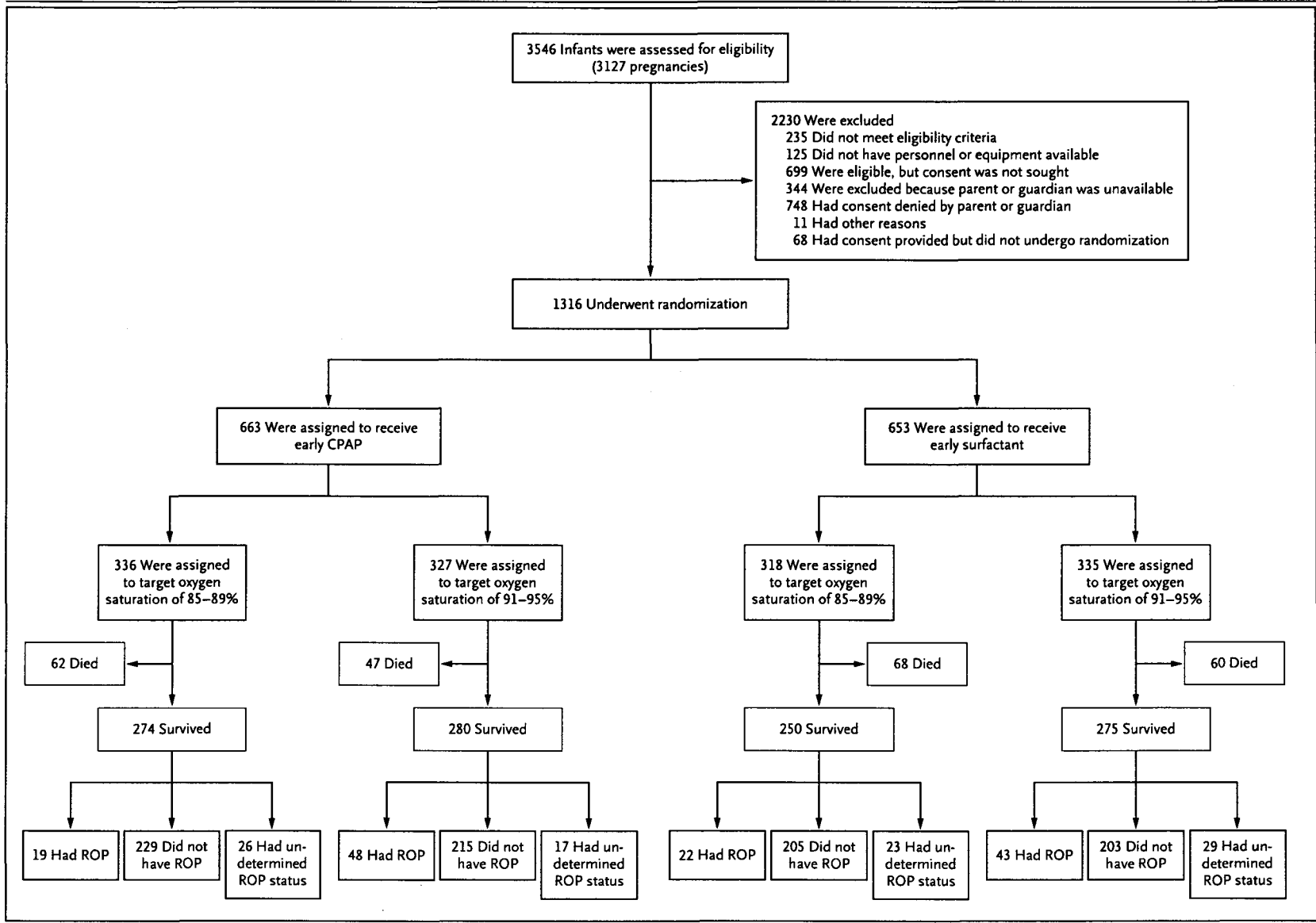


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$; number needed to treat, 11). Although

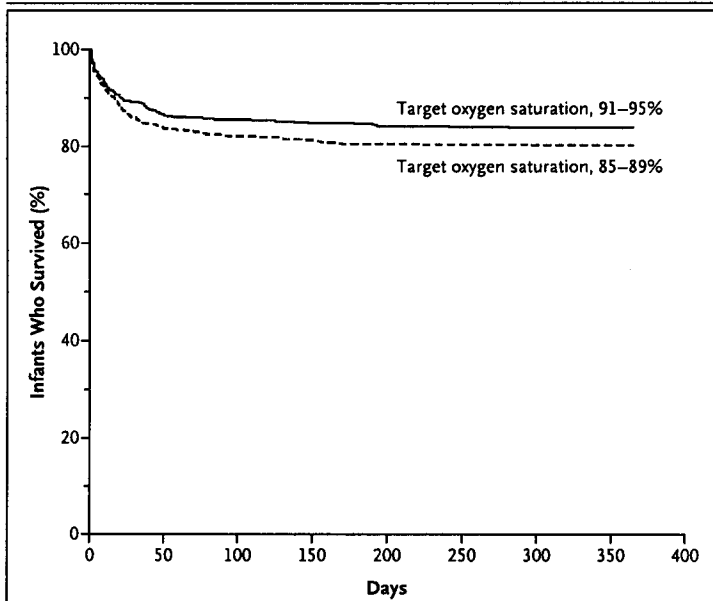


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.

Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

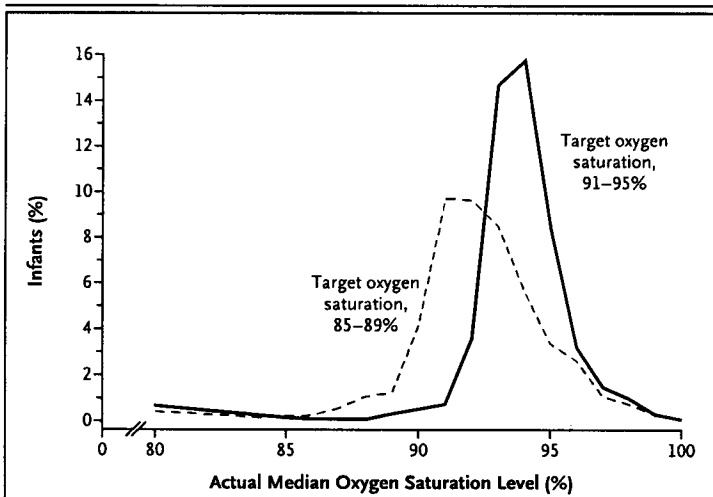


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.

The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO_2 concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Icaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P < 0.001$), required fewer days of mechanical ventilation ($P = 0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P = 0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (F_{iO_2}) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an F_{iO_2} below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an F_{iO_2} of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

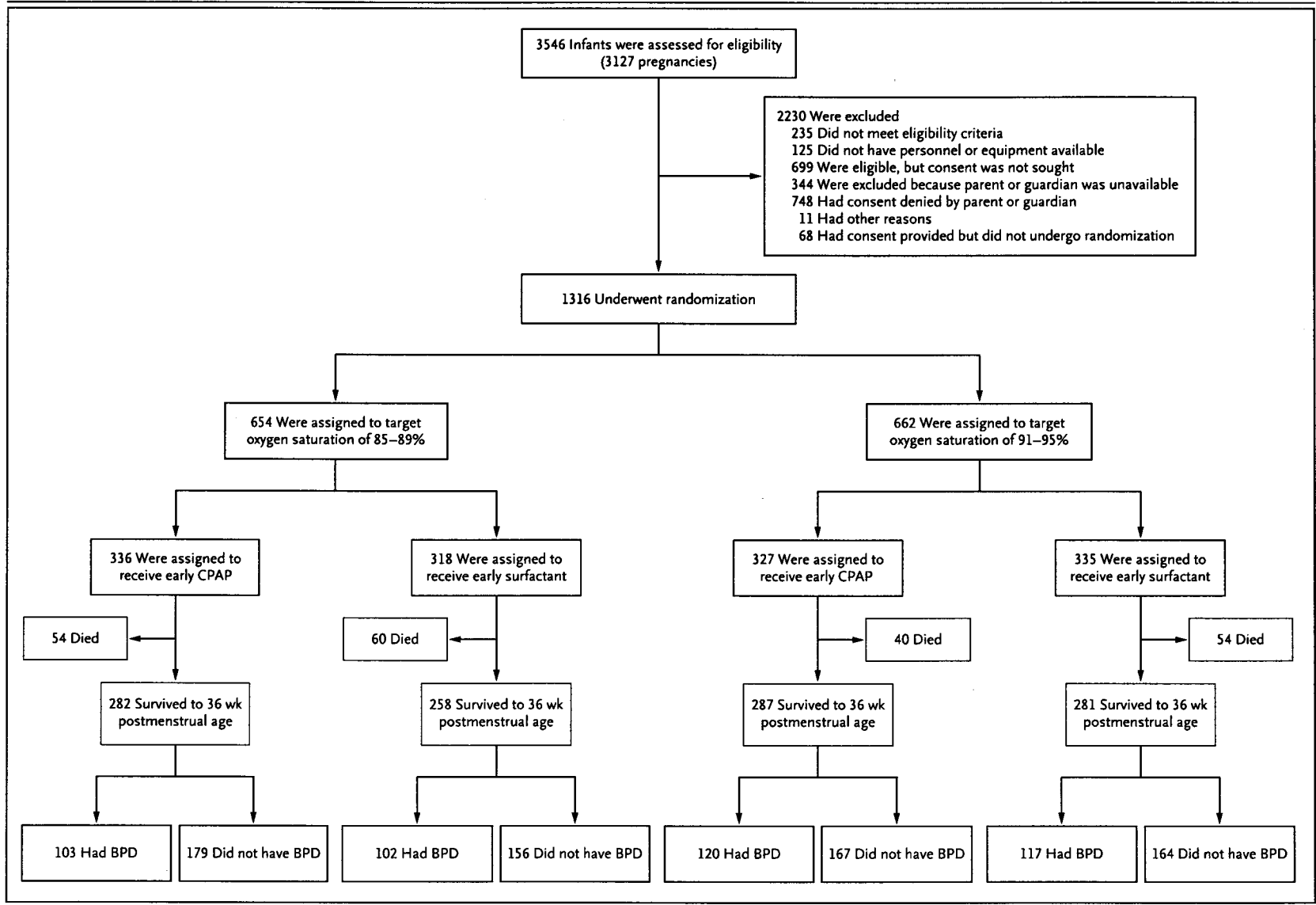


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Variable	CPAP (N = 663) no./total no. (%)	Surfactant (N = 653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the F_{iO_2} to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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U.S. Department of Health and Human Services

NIH News

National Institutes of Health

Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
<http://www.nichd.nih.gov/>

Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition
Early CPAP as Effective For Premies as Ventilator, With Fewer Complications

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by The New England Journal of Medicine. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

The National Institutes of Health (NIH) —The Nation’s Medical Research Agency— includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

From: [Ronald N Goldberg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: SUPPORT Follow Up
Date: Thursday, May 13, 2010 9:44:59 PM

Thank you for your help and support.

Ron

Ronald N. Goldberg, M.D.
Shaad-McBryde Professor of Pediatrics
Chief, Neonatal-Perinatal Medicine
Box 2739
Duke University Medical Center
Durham, NC 27710
Phone: 919-681-6037
Fax: 919-681-6065
email: goldb008@mc.duke.edu

"Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov>

05/13/2010 09:37 PM

To "goldb008@mc.duke.edu" <goldb008@mc.duke.edu>
cc
Subject Re: SUPPORT Follow Up

No joke!

From: Ronald N Goldberg <goldb008@mc.duke.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu May 13 21:12:47 2010
Subject: Re: SUPPORT Follow Up

you're joking, right?

Ronald N. Goldberg, M.D.
Shaad-McBryde Professor of Pediatrics
Chief, Neonatal-Perinatal Medicine
Box 2739
Duke University Medical Center
Durham, NC 27710
Phone: 919-681-6037
Fax: 919-681-6065
email: goldb008@mc.duke.edu

"Higgins, Rosemary
(NIH/NICHD) [E]"

<higginsr@mail.nih.gov>

05/13/2010 03:47 PM

To "goldb008@mc.duke.edu" <goldb008@mc.duke.edu>, Ricki F Goldstein
<golds005@mc.duke.edu>, "cotte010@mc.duke.edu" <cotte010@mc.duke.edu>,
"kim.lutz@duke.edu" <kim.lutz@duke.edu>, "Kimberley.fisher@duke.edu"
<Kimberley.fisher@duke.edu>, "sandra.grimes@duke.edu" <sandra.grimes@duke.edu>
cc "'Gantz, Marie'" <mgantz@rti.org>
Subject SUPPORT Follow Up

CONGRATULATIONS!!!

Your site has no current missing SUPPORT follow up outcomes. Thanks for all the attention to follow up of this important cohort of babies!!!

Thanks for the continued hard work on this study!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Kurt Schibler"
Subject: RE: SUPPORT Follow Up
Date: Thursday, May 13, 2010 4:59:00 PM

You guys do all the work!!!

From: Kurt Schibler [mailto:kurt.schibler@chmcc.org]
Sent: Thursday, May 13, 2010 4:58 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT Follow Up

Rose,

Thanks!! Also, great news on the GDB paper acceptance in Pediatrics. We appreciate your leadership!!

Kurt

On 5/13/10 3:44 PM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> wrote:

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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: "ifrantz@tuftsmedicalcenter.org"; "BMackinnon@tuftsmedicalcenter.org"; "[McGowan, Elisabeth C](#)"; "[Furey, Anne M](#)"
Cc: "[Gantz, Marie](#)"
Subject: SUPPORT FOLLOW UP
Date: Thursday, May 13, 2010 4:14:00 PM

CONGRATULATIONS!!!

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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "goldb008@mc.duke.edu"; "Ricki F.Goldstein"; "cotte010@mc.duke.edu"; "kim.lutz@duke.edu";
"Kimberley.fisher@duke.edu"; "sandra.grimes@duke.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow Up
Date: Thursday, May 13, 2010 3:46:00 PM

CONGRATULATIONS!!!

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Thanks for the continued hard work on this study!!
Rose

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301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "kurt.schibler@cchmc.org"; "Kim Yolton"; "steichji@email.uc.edu"; "Teresa.Gratton@uc.edu"; "Grisby, Cathy (grisbyca)"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow Up
Date: Thursday, May 13, 2010 3:45:00 PM

CONGRATULATIONS!!!

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301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "richard.ehrenkranz@yale.edu"; "monica.konstantino@yale.edu"; "elaine.romano@yale.edu";
"vineet.bhandari@yale.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow Up
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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wacarlo@uab.edu"; "ambal@uab.edu"; "mperalta@peds.uab.edu"; "Shirley Cosby"; "mcollins@peds.uab.edu";
"Vivien Phillips"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow up
Date: Thursday, May 13, 2010 3:43:00 PM

CONGRATULATIONS!!!

Your site has no current missing SUPPORT follow up outcomes. Thanks for all the attention to follow up of this important cohort of babies!!!

This is outstanding given your awesome recruitment!!!

Thanks for the continued hard work on this study!!

Rose

Rosemary D. Higgins, MD
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mcw3@cwru.edu"; "nancy.newman"; "drfjcmd@aol.com"; "Bonnie Siner"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow up
Date: Thursday, May 13, 2010 3:42:00 PM

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Rose

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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo.Sanchez@UTSouthwestern.edu"; "Diana.Vasil@utsouthwestern.edu"; "Roy Heyne";
"Lizette.Torres@utsouthwestern.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT Follow up
Date: Thursday, May 13, 2010 3:41:00 PM

CONGRATULATIONS!!!

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301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Hall, Patricia
To: WCarlo@peds.uab.edu; [Higgins.Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@NIH/NICHD)
Cc: Hall, Patricia
Subject: Doctor Radio interview request
Date: Thursday, May 13, 2010 12:08:33 PM

Hi Dr. Carlo!

I am the producer of Doctor Radio's pediatric program, "On Call for Kids". I'm wondering if you and/or Rosemary Higgins might be available to discuss the NEJM article on Target Ranges of Oxygen Saturation in Extremely Preterm Infants on our next program. The date is Wednesday, May 19th, at 11 am eastern time.

You'd be speaking with my host, Dr. Perri Klass. What I'm thinking is that we start with the study and then open up the discussion to include issues related to premature babies in general. It's a call in program and is geared toward parents—but all couched in terms of how the discussion doesn't take the place of seeing your own doctor.

I'm sure you've heard of Dr. Klass, but if you would like more information about her or the channel, just click on the link below.

I have other dates (the first being June 16th) if the 19th won't work. Just let me know, and thank you!

Best regards,
Patty

Patricia Hall
Producer, Doctor Radio
Sirius 114 and XM 119
Sirius XM Radio
1221 Avenue of the Americas, 19th Floor
New York, NY 10020

O: (212) 584-5325
C: (917) 214-7565

patricia.hall@siriusxm.com

Website: www.sirius.com/doctorradio

-
Please Note:

Our studio is located at the **NYU Langone Medical Center**
550 First Avenue, between 31st and 32nd Streets
New York, NY 10016



From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#); [Gail, Dorothy \(NIH/NHLBI\) \[E\]](#)
Cc: [Kiley, James \(NIH/NHLBI\) \[E\]](#)
Subject: RE: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****
Date: Thursday, May 13, 2010 10:30:04 AM

Dear Rose,

Thanks for all your hardwork on this trial—it is great working with you.

We are looking forward to the noon presentation of SUPPORT at ATS this Sunday.

Carol

Carol J. Blaisdell, M.D.
Medical Officer
Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, May 12, 2010 2:37 PM
To: Blaisdell, Carol (NIH/NHLBI) [E]; Gail, Dorothy (NIH/NHLBI) [E]
Cc: Kiley, James (NIH/NHLBI) [E]
Subject: FW: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****

Hi,

Attached are the SUPPORT press release, both papers and appendices and an editorial written by Colin Morley. The papers and editorial will appear on-line on Sunday.

I want to sincerely thank you and NHLBI for their tremendous support for this study. It is a true pleasure to work with you!!!!

Does anyone have Mary Anne Berberich's contact info? I would like to send her a quick note following Sunday's presentation and release.

I will see all of you on Sunday at ATS.

With warmest regards,
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, May 12, 2010 2:33 PM
To: 'Finer, Neil'; 'Rich, Wade'; 'Gantz, Marie'; 'Nancy Newman'; 'Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu)'; ' (susie.buchter@oz.ped.emory.edu)'; 'Brenda Morris'; 'Laroia, Nirupama'; 'Phelps, Dale'; 'Duara, Shahnaz'; 'Vivek Narendran'; 'vineet.bhandari@yale.edu'; 'Sood, Beena'; 'Michael O`Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; 'Abhik Das'; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu);

'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; cotte010@mc.duke.edu; 'Dennis Wallace'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; 'Kristi Watterberg'; Kurt Schibler [kurt.schibler@cchmc.org]; 'Matthew Bizzarro'; 'Michelle Walsh'; 'Mickey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; 'Roger Faix'; 'Ronald GOLdberg'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; VanMeurs, Krisa

Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Cunningham, Meg'; 'Huitema, Carolyn Petrie'

Subject: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****

Hello again everyone:

I have several items regarding SUPPORT.

Both manuscripts are attached along with the appendices.

The authors appear at the end of the paper as formal “authors” due to space limits from NEJM. I have also attached the NIH press release for the papers. Finally, there is an editorial which will appear on-line and in the May 27 issue of NEJM.

ALL OF THIS INFORMATION IS SUBJECT TO EMBARGO RULES AND NOT TO BE RELEASED UNTIL SUNDAY MAY 16 at 1 PM ET. This information can be *confidentially shared with your institutional press/public affairs office* as long as the embargo is respected.

Thanks to everyone at each and every site for all of the hard work and effort on this study. A special appreciation of gratitude goes to the coordinators who really went above and beyond to get the patients enrolled in this difficult study.

**A very, very special and heart felt thanks to
Neil and Wally for all of their hard work,
commitment, effort and patience to bring this
to completion!!!!**

**Both SUPPORT Papers will be *accelerated Online First release*
scheduled to coincide with the presentations of the results at the
American Thoracic Society's annual meeting on Sunday May 16,
2010. The on-line release will occur at 1 PM EDT on 5/16/2010.
The print publication is slated to appear in the May 27, 2010 issue
of NEJM.**

If you have any questions, please contact me

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

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MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: NEJM
Date: Thursday, May 13, 2010 8:42:01 AM

Did you send NEJM the form about submitting the articles to PubMed Central?

From: Higgins, Rosemary (NIH/NICHHD) [E]
To: Gail, Dorothy (NIH/NHLBI) [E]
Subject: RE: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****
Date: Thursday, May 13, 2010 8:42:00 AM

Again
Thanks for all the support!
Rose

From: Gail, Dorothy (NIH/NHLBI) [E]
Sent: Wednesday, May 12, 2010 5:42 PM
To: Higgins, Rosemary (NIH/NICHHD) [E]
Subject: RE: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****

THANK YOU ROSE FOR YOUR FANTASTIC LEADERSHIP ON SUPPORT.

I do not have Mary Anne's email.

Congratulations!

From: Higgins, Rosemary (NIH/NICHHD) [E]
Sent: Wednesday, May 12, 2010 2:37 PM
To: Blaisdell, Carol (NIH/NHLBI) [E]; Gail, Dorothy (NIH/NHLBI) [E]
Cc: Kiley, James (NIH/NHLBI) [E]
Subject: FW: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****

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Sent: Wednesday, May 12, 2010 2:33 PM
To: 'Finer, Neil'; 'Rich, Wade'; 'Gantz, Marie'; 'Nancy Newman'; 'Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu)'; ' (susie.buchter@oz.ped.emory.edu)'; 'Brenda Morris'; 'Laroia, Nirupama'; 'Phelps, Dale'; 'Duara, Shahnaz'; 'Vivek Narendran';

'vineet.bhandari@yale.edu'; 'Sood, Beena'; 'Michael O` Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; 'Abhik Das'; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; cotte010@mc.duke.edu; 'Dennis Wallace'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; 'Kristi Watterberg'; Kurt Schibler [kurt.schibler@cchmc.org]; 'Matthew Bizzarro'; 'Michelle Walsh'; 'Mickey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; 'Roger Faix'; 'Ronald GOLDBERG'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Cunningham, Meg'; 'Huitema, Carolyn Petrie'
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Rose

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higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@NIH/NICHD)
To: ["Webb, Robin E."](mailto:Webb.Robin.E)
Subject: RE: SUPPORT data queries
Date: Thursday, May 13, 2010 8:39:00 AM

From: Webb, Robin E. [<mailto:rwebb@rti.org>]
Sent: Wednesday, May 12, 2010 7:26 PM
To: alaptook@WIHRI.org; Bradley Yoder; adas@rti.org; mgantz@rti.org; Higgins, Rosemary (NIH/NICHD) [E]; kurt.schibler@cchmc.org; mcw3@cwru.edu; nancy newman; nfiner@ucsd.edu; Roger.Faix@hsc.utah.edu; Wallace, Dennis; Wally Carlo, M.D.; wrich@ucsd.edu
Cc: sharon.gough@hsc.utah.edu; Archer, Stephanie (NIH/NICHD) [E]; Brenda Vecchio; Cunningham, Meg; fmartinez@ucsd.edu; Huitema, Carolyn Petrie; Zaterka-Baxter, Kristin; Starlett Williams; Webb, Robin E.
Subject: SUPPORT data queries

We need to schedule a call to discuss the attached. Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin Webb
RTI, International
6110 Executive Blvd, Suite 902
Rockville, MD 20852

Mon 5/24 ok except 12-1
Wed 5/26 open
Thurs 5/27 open

Tues 6/1 open
Wed 6/2 open except 3-4

Wed 6/9 open
Thurs 6/10 open
Fri 6/11 open except 230-4

Mon 6/14 open
Tues 6/15 open
Wed 6/16 open until noon
Thurs 6/17 open except 2-330
Fri 6/18 open except 10-11

Mon 6/21 open except 3-4
Tues 6/22 open
Wed 6/23 open
Thurs 6/24 open except 2-3
Fri 6/25 (I may take this day off)

Mon 6/28 open
Tues 6/29 open except 2-3
Wed 6/30 open

Thurs 7/1 open except 130-3
Fri 7/2 open

From: [Avroy Fanaroff](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****
Date: Wednesday, May 12, 2010 2:48:21 PM

Great effort
Congratulations all around
Av

On Wed, May 12, 2010 at 2:33 PM, Higgins, Rosemary (NIH/NICHD) [E]
<higginsr@mail.nih.gov> wrote:

> Hello again everyone:

>

>

>

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>

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>

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> coincide with the presentations of the results at the American Thoracic
> Society's annual meeting on Sunday May 16, 2010. The on-line release will
> occur at 1 PM EDT on 5/16/2010. The print publication is slated to appear
> in the May 27, 2010 issue of NEJM.

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> If you have any questions, please contact me
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: Blaisdell, Carol (NIH/NHLBI) [E]; Gail, Dorothy (NIH/NHLBI) [E]
Cc: Kiley, James (NIH/NHLBI) [E]
Subject: FW: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****
Date: Wednesday, May 12, 2010 2:37:00 PM
Attachments: [SUPPORT Press release.docx](#)
[Carlo.pdf](#)
[Carlo_supapp.pdf](#)
[Finer.pdf](#)
[Finer_supapp.pdf](#)
[Morley.pdf](#)

Hi,

Attached are the SUPPORT press release, both papers and appendices and an editorial written by Colin Morley. The papers and editorial will appear on-line on Sunday.

I want to sincerely thank you and NHLBI for their tremendous support for this study. It is a true pleasure to work with you!!!!

Does anyone have Mary Anne Berberich's contact info? I would like to send her a quick note following Sunday's presentation and release.

I will see all of you on Sunday at ATS.

With warmest regards,
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, May 12, 2010 2:33 PM
To: 'Finer, Neil'; 'Rich, Wade'; 'Gantz, Marie'; 'Nancy Newman'; 'Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu)'; ' (susie.buchter@oz.ped.emory.edu)'; 'Brenda Morris'; 'Laroia, Nirupama'; 'Phelps, Dale'; 'Duara, Shahnaz'; 'Vivek Narendran'; 'vineet.bhandari@yale.edu'; 'Sood, Beena'; 'Michael O` Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; 'Abhik Das'; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; cotte010@mc.duke.edu; 'Dennis Wallace'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; 'Kristi Watterberg'; Kurt Schibler [kurt.schibler@cchmc.org]; 'Matthew Bizzarro'; 'Michelle Walsh'; 'MIckey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; 'Roger Faix'; 'Ronald GOLdberg'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Cunningham, Meg'; 'Huitema, Carolyn Petrie'
Subject: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****

Hello again everyone:

I have several items regarding SUPPORT.

Both manuscripts are attached along with the appendices.

The authors appear at the end of the paper as formal “authors” due to space limits from NEJM. I have also attached the NIH press release for the papers. Finally, there is an editorial which will appear on-line and in the May 27 issue of NEJM.

ALL OF THIS INFORMATION IS SUBJECT TO EMBARGO RULES AND NOT TO BE RELEASED UNTIL SUNDAY MAY 16 at 1 PM ET. This information can be *confidentially shared with your institutional press/public affairs office* as long as the embargo is respected.

Thanks to everyone at each and every site for all of the hard work and effort on this study. A special appreciation of gratitude goes to the coordinators who really went above and beyond to get the patients enrolled in this difficult study.

A very, very special and heart felt thanks to Neil and Wally for all of their hard work, commitment, effort and patience to bring this to completion!!!!

Both SUPPORT Papers will be *accelerated Online First release* scheduled to coincide with the presentations of the results at the American Thoracic Society’s annual meeting on Sunday May 16,

**2010. The on-line release will occur at 1 PM EDT on 5/16/2010.
The print publication is slated to appear in the May 27, 2010 issue
of NEJM.**

If you have any questions, please contact me

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Rosemary D. Higgins, MD

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U.S. Department of Health and Human Services

NIH News

National Institutes of Health

Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
<http://www.nichd.nih.gov/>

Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

Contact:

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition *Early CPAP as Effective For Premies as Ventilator, With Fewer Complications*

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by *The New England Journal of Medicine*. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

The National Institutes of Health (NIH) —The Nation’s Medical Research Agency— includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

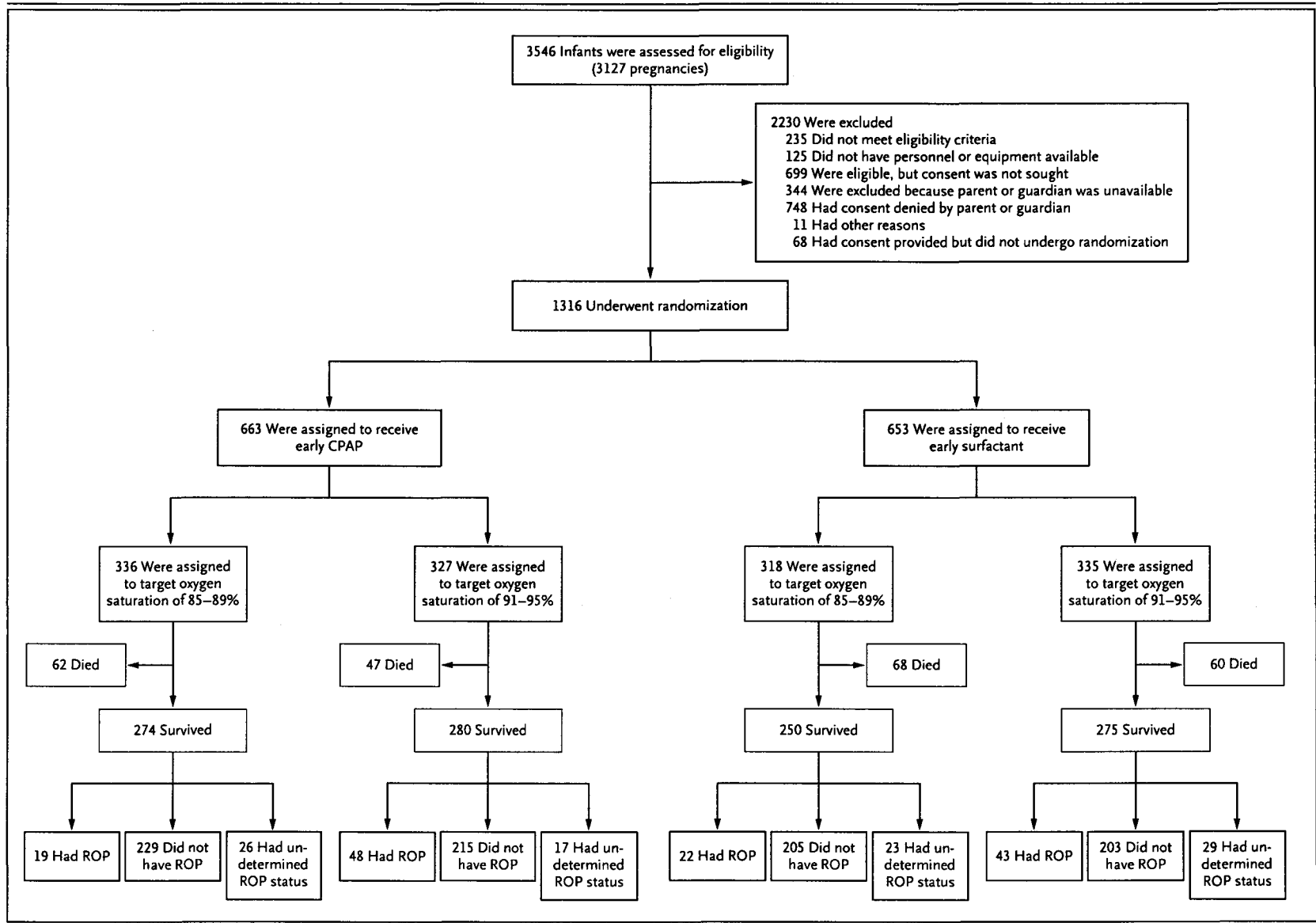


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$; number needed to treat, 11). Although

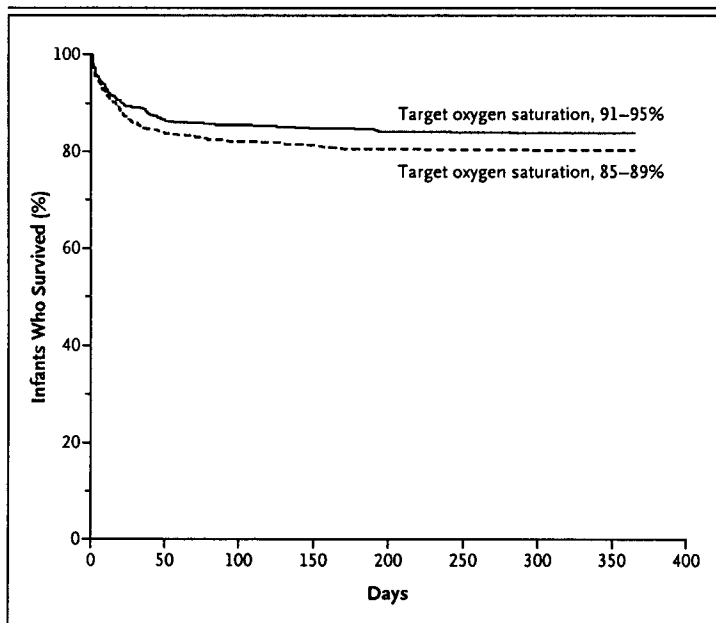


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.
 Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

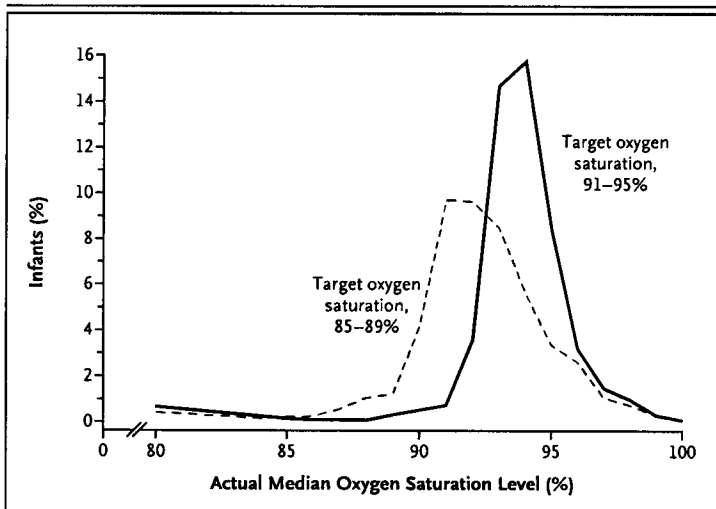


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.
 The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the F_{iO_2} concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikarria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911781.

Appendix Table 1: Cause of Death in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth

Weight Infants

Category – no./total no. (%)	Lower Saturation	Higher Saturation
	Group	Group
	n/N (%)	n/N (%)
Respiratory distress syndrome	31/130 (23.8)	31/107 (29.0)
Infection	25/130 (19.2)	21/107 (19.6)
Necrotizing enterocolitis	23/130 (17.7)	14/107 (13.1)
Bronchopulmonary dysplasia	14/130 (10.8)	10/107 (9.3)
Central nervous system insult	12/130 (9.2)	9/107 (8.4)
Immaturity	7/130 (5.4)	3/107 (2.8)
Other	18/130 (13.8)	19/107 (17.8)
Causes of death did not differ		

Appendix Table 2: Effect of Retinopathy Adjudication for Low vs. High Oxygen Saturation Target Groups

Characteristic	Lower Saturation	Higher Saturation	Relative Risk for	Adjusted
	Group (N=654)	Group (N=662)	Low SpO ₂ vs. High SpO ₂ (95% CI)	P value
	n/N (%)	n/N (%)		
Severe retinopathy/death, All outcomes (non-adjudicated)	171/605 (28.3)	198/616 (32.1)	0.9 (0.76, 1.06)	0.205
Severe retinopathy among survivors, All outcomes (non-adjudicated)	41/475 (8.6)	91/509 (17.9)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed by majority rule*	171/642 (26.6)	198/656 (30.2)	0.91 (0.77, 1.07)	0.253
Severe retinopathy among survivors, Cases considered confirmed by majority rule*	41/512 (8.0)	91/549 (16.6)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed majority rule* when "unknown cases" considered to have severe retinopathy†	183/654 (28.0)	204/662 (30.8)	0.93 (0.79, 1.1)	0.412
Severe retinopathy among survivors, Cases confirmed by majority rule when "unknown cases" considered to have severe retinopathy†	53/524 (10.1)	97/555 (17.5)	0.62 (0.45, 0.84)	0.002

Relative risks are adjusted for gestational age stratification, center, and familial clustering;

*Majority rule: If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; If two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=missing.

†If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; if two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=Y.

Appendix Table 3. Other Outcomes in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low

Birth Weight Infants

Outcome	Lower Saturation Group	Higher Saturation Group	Adjusted P value [§]
Length of stay any hospital, (days) m±SE*	104.5 ± 2.0	106.4 ± 2.0	0.45
Length of stay at study hospital, (days) m±SE*	99.8 ± 2.0	103.0 ± 2.0	0.22
Duration of mechanical ventilation, (days) m±SE [†]	25.5 ± 1.1	26.9 ± 1.0	0.30
Duration of oxygen supplementation, (days) m±SE [†]	59.8 ± 1.6	67.4 ± 1.5	<0.001
Continuous positive airway pressure, (days) m±SE [†]	17.1 ± 0.6	17.0 ± 0.6	0.94
Nasal synchronized intermittent mandatory ventilation, (days) m±SE [†]	3.3 ± 0.3	3.8 ± 0.3	0.14
Alive off mechanical ventilation by day 14, (days) – no. (%)	332/644 (51.6)	326/655 (49.8)	0.86
Alive off mechanical ventilation by day 7, (days) – no. (%)	351/648 (54.2)	329/659 (49.9)	0.27
Percent of time in actual oxygen saturation range 84-96%, (%) m±SD [‡]	66.9 ± 13.9	68.0 ± 15.2	0.16 [¶]

*Among survivors to discharge, transfer or one year; maximum value is 366 days

[†]Among survivors to discharge, transfer or 120 days; maximum value is 120 days

[‡]Percent of time based only on total time on oxygen supplementation

§Adjusted for stratification factors (study center, gestational age group) as well as for familial clustering

¶Unadjusted P value

ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P < 0.001$), required fewer days of mechanical ventilation ($P = 0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P = 0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (F_{iO_2}) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an F_{iO_2} below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an F_{iO_2} of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

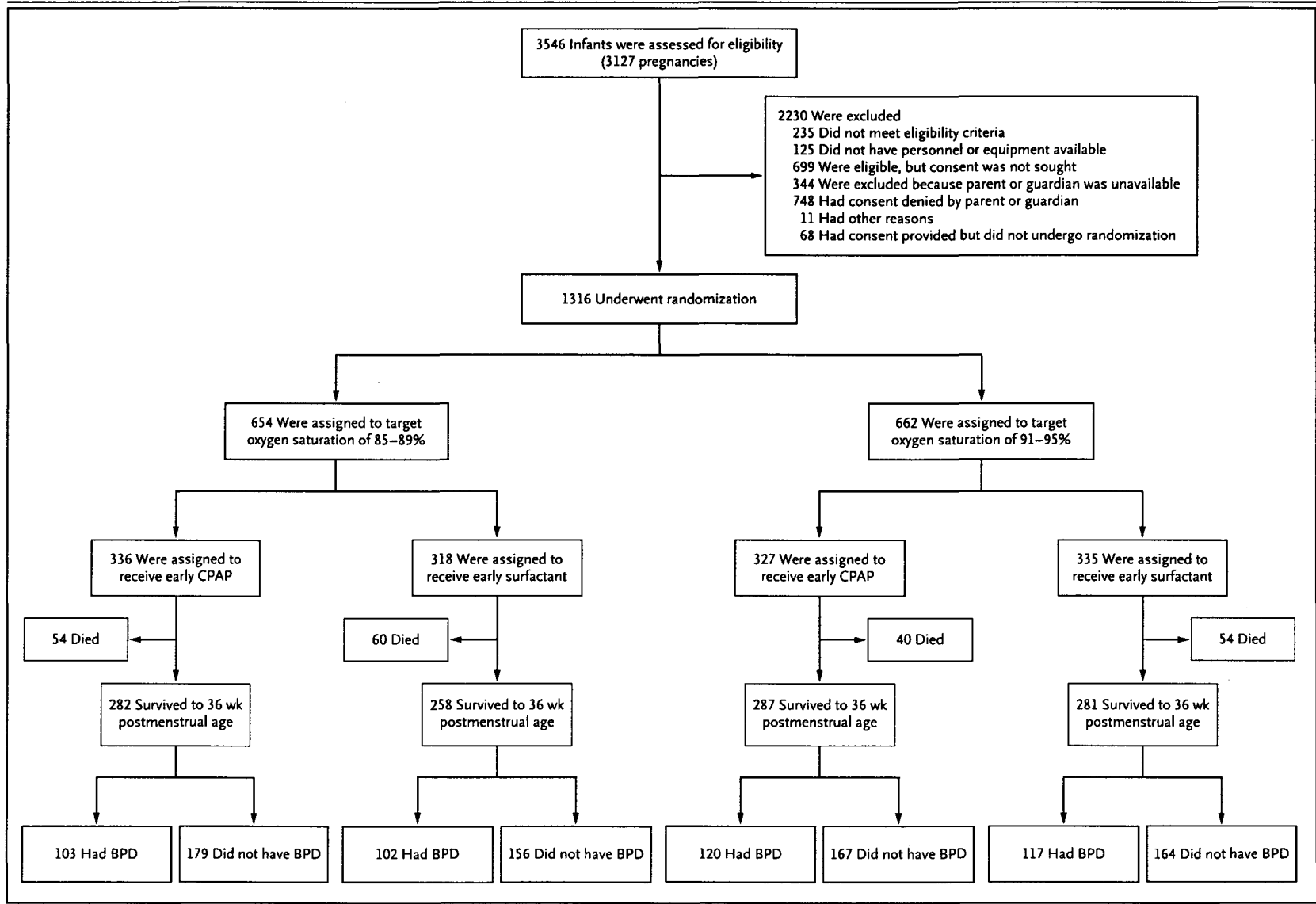


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Variable	CPAP (N = 663) no./total no. (%)	Surfactant (N = 653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010. DOI: 10.1056/NEJMoa0911783.

Web Appendix Tables

Table A1. Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted	35.8 ± 1.5	38.7 ± 1.6	-3.0 (-7.2, 1.3)	0.17
Mean±StdErr, Unadjusted Median (IQR) (N=421)	29.5 (10, 48)	33 (14, 56)		
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

Table A2. Cause of Death for 24 to 25 week stratum

Contributory Cause of Death	CPAP (N=68)	Surfactant (N=90)
Respiratory distress syndrome	13/68 (19.1)	31/90 (34.4)
Bronchopulmonary dysplasia	10/68 (14.7)	7/90 (7.8)
Infection	14/68 (20.6)	15/90 (16.7)
Necrotizing enterocolitis	10/68 (14.7)	16/90 (17.8)
Central nervous center insult	11/68 (16.2)	5/90 (5.6)
Immaturity	3/68 (4.4)	5/90 (5.6)
Other	7/68 (10.3)	11/90 (12.2)

Table A3. Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P-value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; $P=0.30$). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) ($P<0.001$ for both comparisons), and required ventilation for an average of 3 days less ($P=0.03$). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the F_iO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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Subject: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS AND EMBARGO*****
Date: Wednesday, May 12, 2010 2:33:00 PM
Attachments: SUPPORT Press release.docx
Carlo.pdf
Carlo_supapp.pdf
Finer.pdf
Finer_supapp.pdf
Morley.pdf

Hello again everyone:

I have several items regarding SUPPORT.

Both manuscripts are attached along with the appendices.

The authors appear at the end of the paper as formal "authors" due to space limits from NEJM. I have also attached the NIH press release for the papers. Finally, there is an editorial which will appear on-line and in the May 27 issue of NEJM.

ALL OF THIS INFORMATION IS SUBJECT TO EMBARGO RULES AND NOT TO BE RELEASED UNTIL SUNDAY MAY 16 at 1 PM ET. This information can be *confidentially shared with your institutional press/public affairs office* as long as the embargo is respected.

Thanks to everyone at each and every site for all of the hard work and effort on this study. A special appreciation of gratitude goes to the

coordinators who really went above and beyond to get the patients enrolled in this difficult study.

A very, very special and heart felt thanks to Neil and Wally for all of their hard work, commitment, effort and patience to bring this to completion!!!!

Both SUPPORT Papers will be *accelerated Online First* release scheduled to coincide with the presentations of the results at the American Thoracic Society's annual meeting on Sunday May 16, 2010. The on-line release will occur at 1 PM EDT on 5/16/2010. The print publication is slated to appear in the May 27, 2010 issue of NEJM.

If you have any questions, please contact me

Rose

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U.S. Department of Health and Human Services

NIH News

National Institutes of Health

Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
<http://www.nichd.nih.gov/>

Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition *Early CPAP as Effective For Premies as Ventilator, With Fewer Complications*

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by *The New England Journal of Medicine*. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

The National Institutes of Health (NIH) —The Nation’s Medical Research Agency— includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.
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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

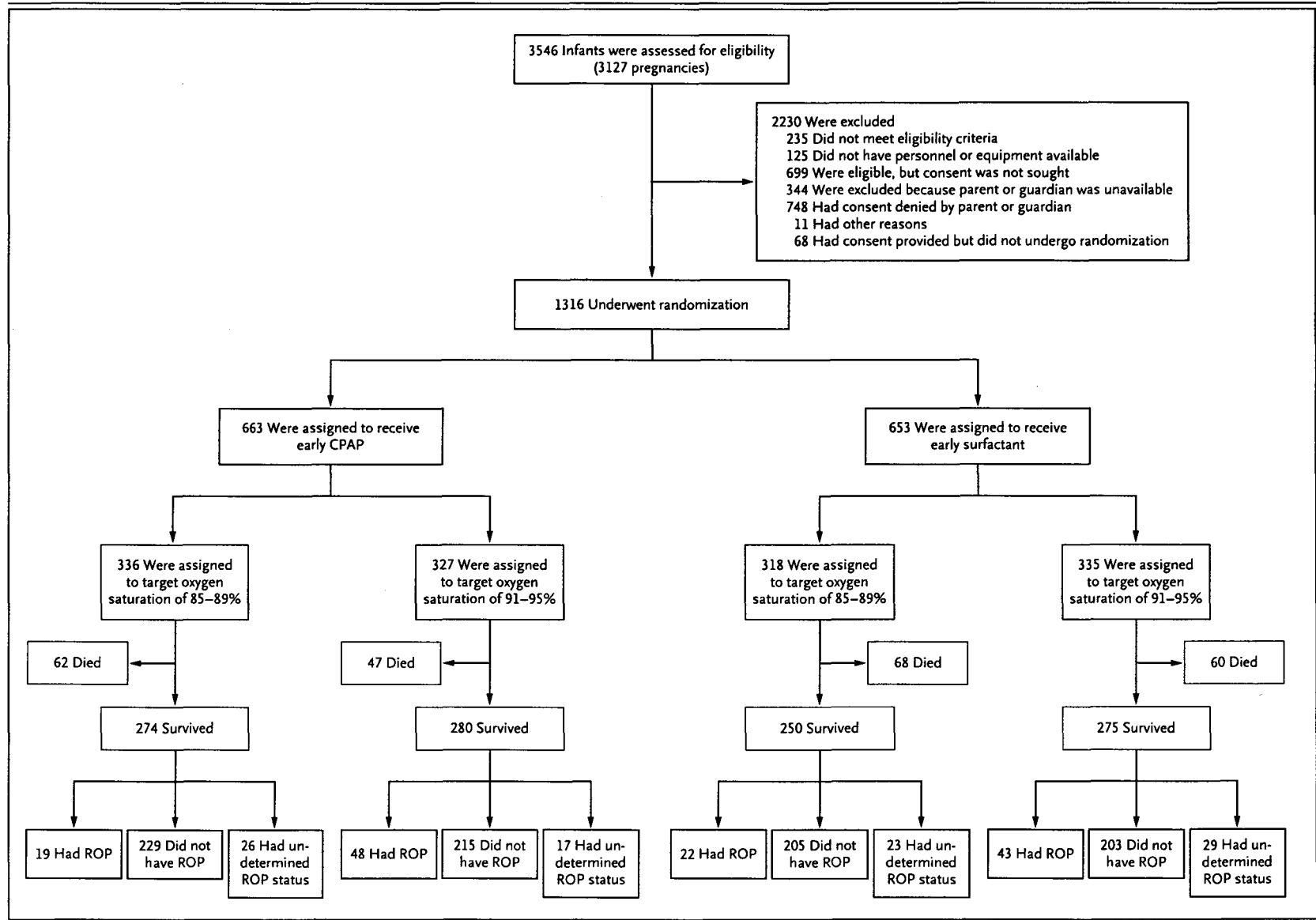


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; P<0.001; number needed to treat, 11). Although

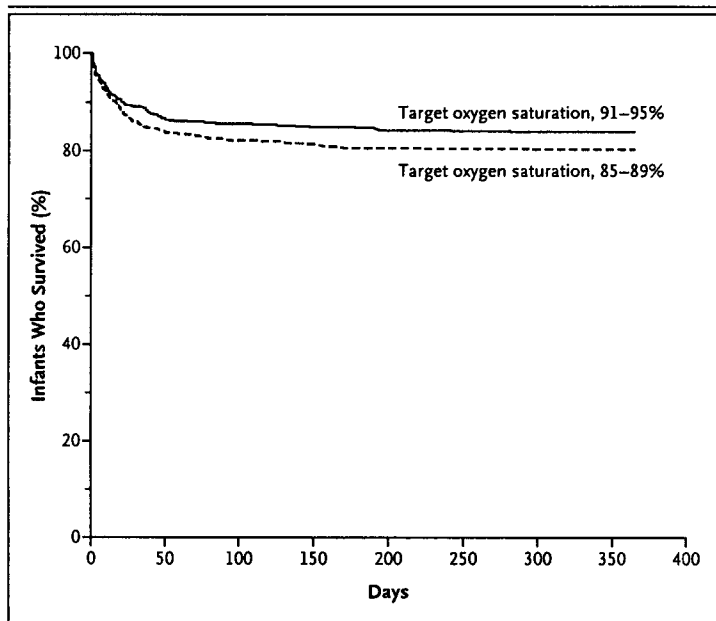


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.
 Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

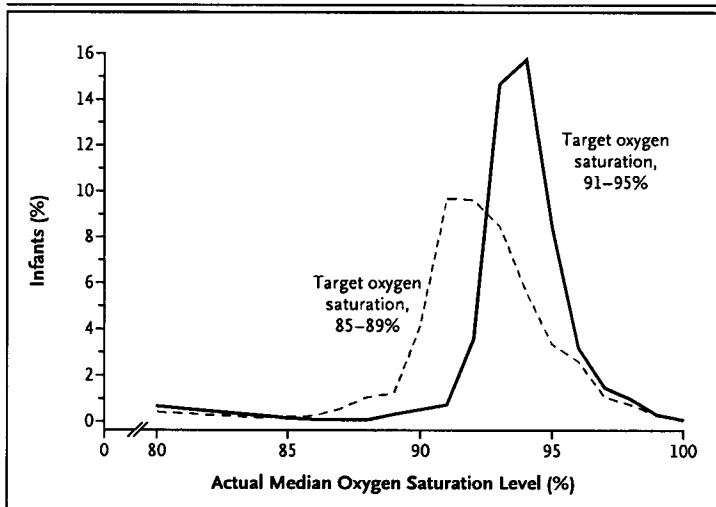


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.
 The medians of the distributions were significantly different on the basis of a rank-sum test (P<0.001). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (P=0.002), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO₂ concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911781.

Appendix Table 1: Cause of Death in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth

Weight Infants

Category – no./total no. (%)	Lower Saturation	Higher Saturation
	Group	Group
	n/N (%)	n/N (%)
Respiratory distress syndrome	31/130 (23.8)	31/107 (29.0)
Infection	25/130 (19.2)	21/107 (19.6)
Necrotizing enterocolitis	23/130 (17.7)	14/107 (13.1)
Bronchopulmonary dysplasia	14/130 (10.8)	10/107 (9.3)
Central nervous system insult	12/130 (9.2)	9/107 (8.4)
Immaturity	7/130 (5.4)	3/107 (2.8)
Other	18/130 (13.8)	19/107 (17.8)
Causes of death did not differ		

Appendix Table 2: Effect of Retinopathy Adjudication for Low vs. High Oxygen Saturation Target Groups

Characteristic	Lower Saturation	Higher Saturation	Relative Risk for	Adjusted
	Group (N=654)	Group (N=662)	Low SpO ₂ vs. High	P value
	n/N (%)	n/N (%)	SpO ₂ (95% CI)	
Severe retinopathy/death, All outcomes (non-adjudicated)	171/605 (28.3)	198/616 (32.1)	0.9 (0.76, 1.06)	0.205
Severe retinopathy among survivors, All outcomes (non-adjudicated)	41/475 (8.6)	91/509 (17.9)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed by majority rule*	171/642 (26.6)	198/656 (30.2)	0.91 (0.77, 1.07)	0.253
Severe retinopathy among survivors, Cases considered confirmed by majority rule*	41/512 (8.0)	91/549 (16.6)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed majority rule* when "unknown cases" considered to have severe retinopathy†	183/654 (28.0)	204/662 (30.8)	0.93 (0.79, 1.1)	0.412
Severe retinopathy among survivors, Cases confirmed by majority rule when "unknown cases" considered to have severe retinopathy†	53/524 (10.1)	97/555 (17.5)	0.62 (0.45, 0.84)	0.002

Relative risks are adjusted for gestational age stratification, center, and familial clustering;

*Majority rule: If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; If two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=missing.

†If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; if two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=Y.

Appendix Table 3. Other Outcomes in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low

Birth Weight Infants

Outcome	Lower Saturation Group	Higher Saturation Group	Adjusted P value [§]
Length of stay any hospital, (days) m±SE*	104.5 ± 2.0	106.4 ± 2.0	0.45
Length of stay at study hospital, (days) m±SE*	99.8 ± 2.0	103.0 ± 2.0	0.22
Duration of mechanical ventilation, (days) m±SE [†]	25.5 ± 1.1	26.9 ± 1.0	0.30
Duration of oxygen supplementation, (days) m±SE [†]	59.8 ± 1.6	67.4 ± 1.5	<0.001
Continuous positive airway pressure, (days) m±SE [†]	17.1 ± 0.6	17.0 ± 0.6	0.94
Nasal synchronized intermittent mandatory ventilation, (days) m±SE [†]	3.3 ± 0.3	3.8 ± 0.3	0.14
Alive off mechanical ventilation by day 14, (days) – no. (%)	332/644 (51.6)	326/655 (49.8)	0.86
Alive off mechanical ventilation by day 7, (days) – no. (%)	351/648 (54.2)	329/659 (49.9)	0.27
Percent of time in actual oxygen saturation range 84-96%, (%) m±SD [‡]	66.9 ± 13.9	68.0 ± 15.2	0.16 [¶]

*Among survivors to discharge, transfer or one year; maximum value is 366 days

[†]Among survivors to discharge, transfer or 120 days; maximum value is 120 days

[‡]Percent of time based only on total time on oxygen supplementation

§Adjusted for stratification factors (study center, gestational age group) as well as for familial clustering

¶Unadjusted P value

ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P<0.001$), required fewer days of mechanical ventilation ($P=0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P=0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.
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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (F_{iO_2}) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an F_{iO_2} below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an F_{iO_2} of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

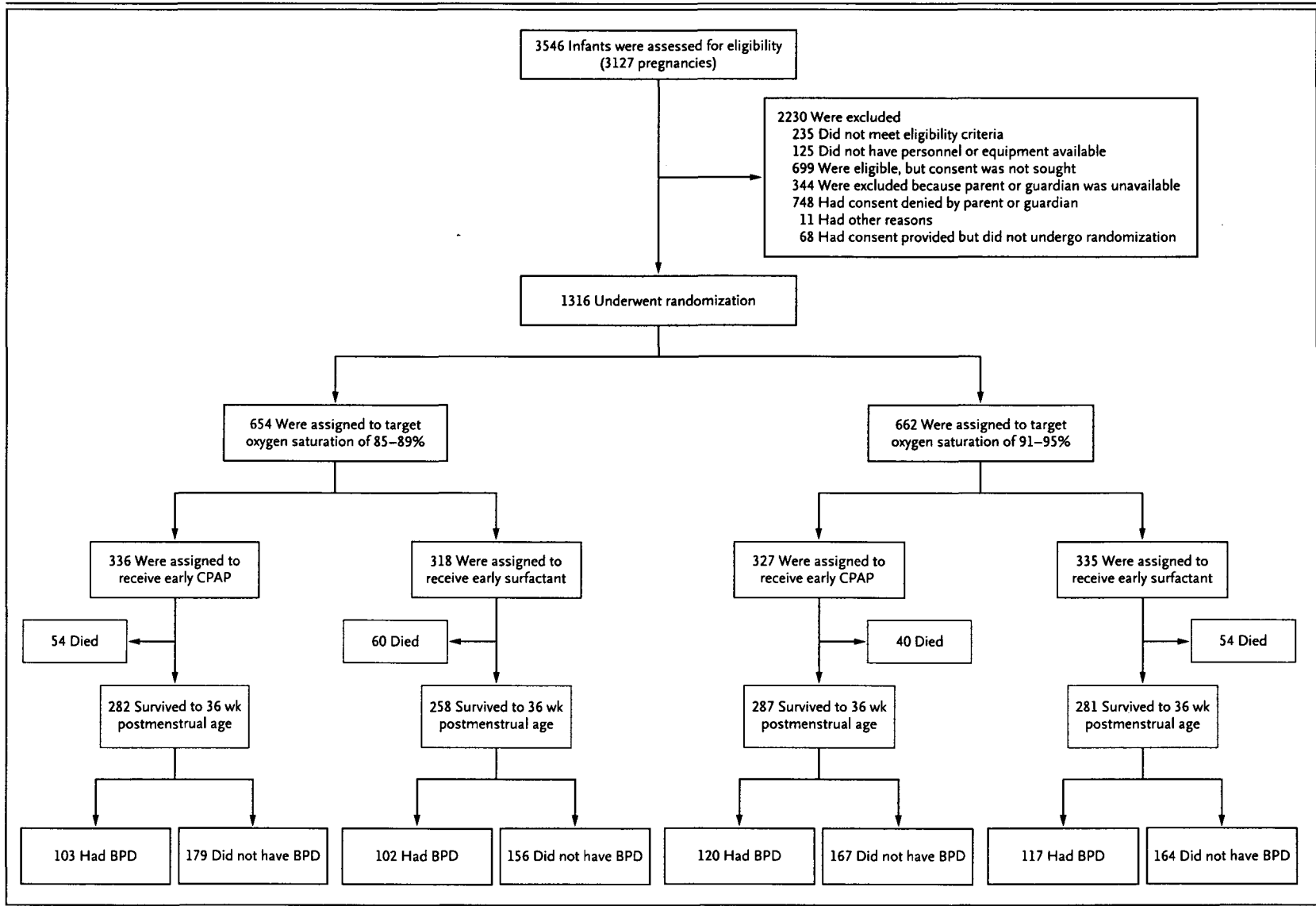


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N=663)	Surfactant (N=653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Table 2. Apgar Scores of Newborns and Interventions in the Delivery Room and NICU.*

Variable	CPAP (N = 663) no./total no. (%)	Surfactant (N = 653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N = 663)	Surfactant (N = 653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911783.

Web Appendix Tables

Table A1. Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted	35.8 ± 1.5	38.7 ± 1.6	-3.0 (-7.2, 1.3)	0.17
Mean±StdErr, Unadjusted Median (IQR) (N=421)	29.5 (10, 48)	33 (14, 56)		
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

Table A2. Cause of Death for 24 to 25 week stratum

Contributory Cause of Death	CPAP (N=68)	Surfactant (N=90)
Respiratory distress syndrome	13/68 (19.1)	31/90 (34.4)
Bronchopulmonary dysplasia	10/68 (14.7)	7/90 (7.8)
Infection	14/68 (20.6)	15/90 (16.7)
Necrotizing enterocolitis	10/68 (14.7)	16/90 (17.8)
Central nervous center insult	11/68 (16.2)	5/90 (5.6)
Immaturity	3/68 (4.4)	5/90 (5.6)
Other	7/68 (10.3)	11/90 (12.2)

Table A3. Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P-value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the FiO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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Thanks very much for the information. Enclosed is my contact information. I am copying this to Dr. Rose Higgins at the NIH who probably should be the other contact person rather than our institution's press office.

Wally

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From: Zeis, Jennifer [mailto:jzeis@nejm.org]
Sent: Tuesday, April 20, 2010 11:37 AM
To: Wally Carlo, M.D.
Subject: Online First release schedule for NEJM 09-11781

Dear Dr. Carlo,

As you know, your NEJM Original Article is on an accelerated Online First release schedule to coincide with your presentation of the results at the American Thoracic Society's annual meeting. I am writing to share the details of that schedule and to request your preferred media points of contact.

We will provide your article to reporters at 10 AM EDT Thursday, May 13. When we provide your article to the media under embargo, we will post the material on our password-protected NEJM Media Center, where only journalists who have agreed to respect our embargo may access it. I will email you this final file and any related material at that time

Your article will be embargoed until 1 PM EDT Sunday, May 16, the start of your ATS presentation on the trial. The ATS and NEJM embargoes are coordinated to lift simultaneously so you may reference your NEJM publication at the meeting, if you wish. Your paper will be published on NEJM.org as soon as the embargo lifts, and will later be published in the May 27 printed issue.

And finally, please let me know what **contact information you would like me to provide to journalists** who wish to interview you and/or your co-authors. You may include your institution's press office in addition to, or instead of, your personal contact information.

Many thanks. If you have any questions, please don't hesitate to ask.

Best regards,
Jen Zeis

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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-

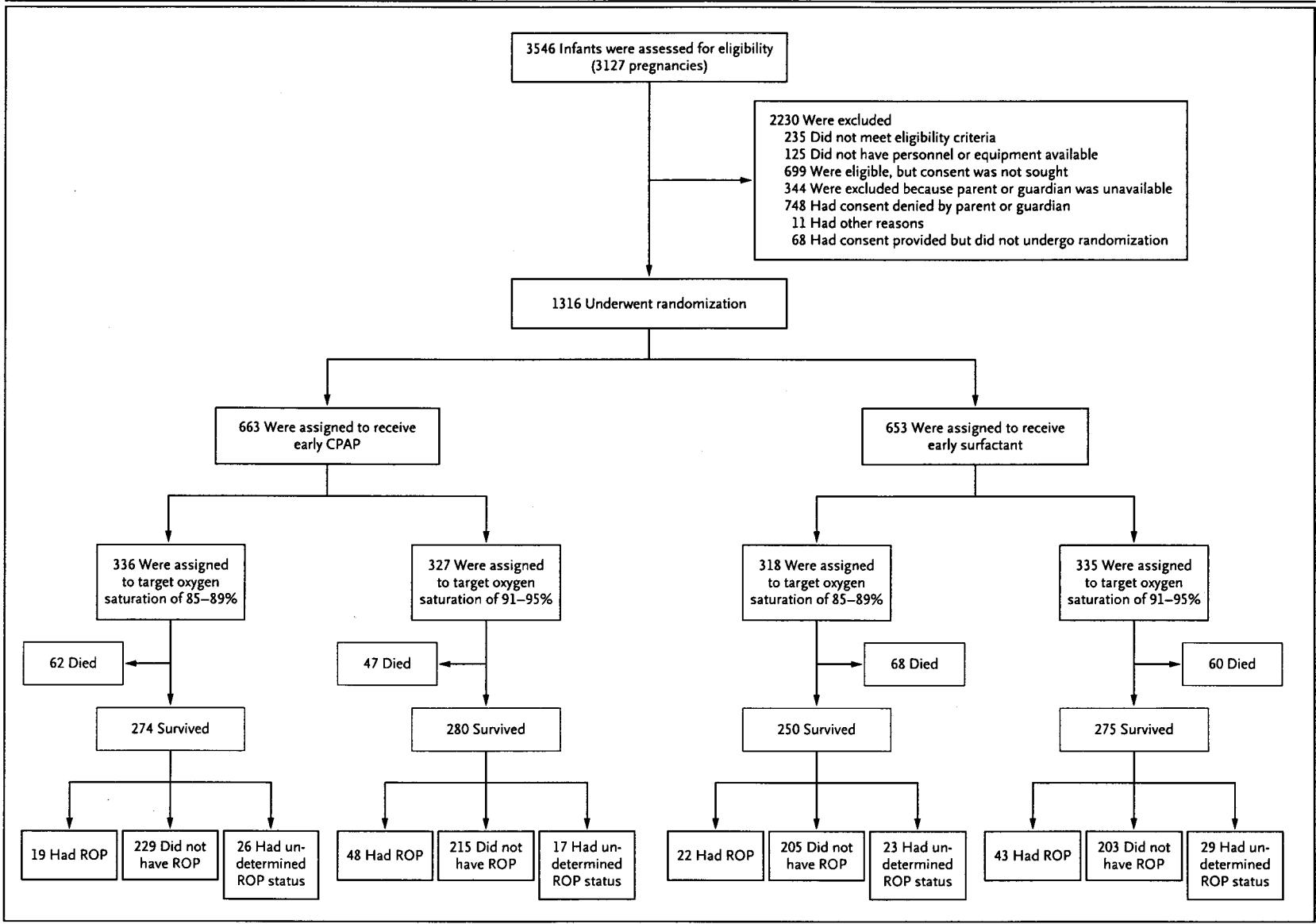


Table 1. Baseline Characteristics of the Patients.

Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien–Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; P<0.001; number needed to treat, 11). Although

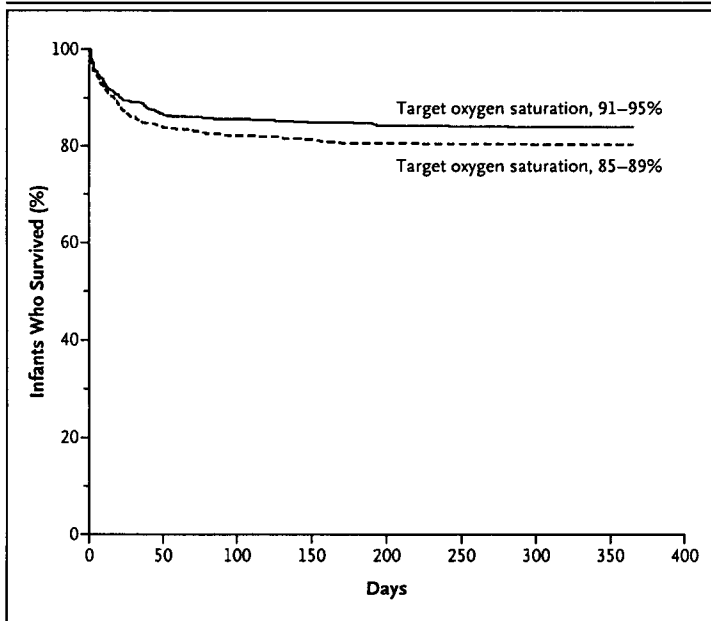


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.

Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

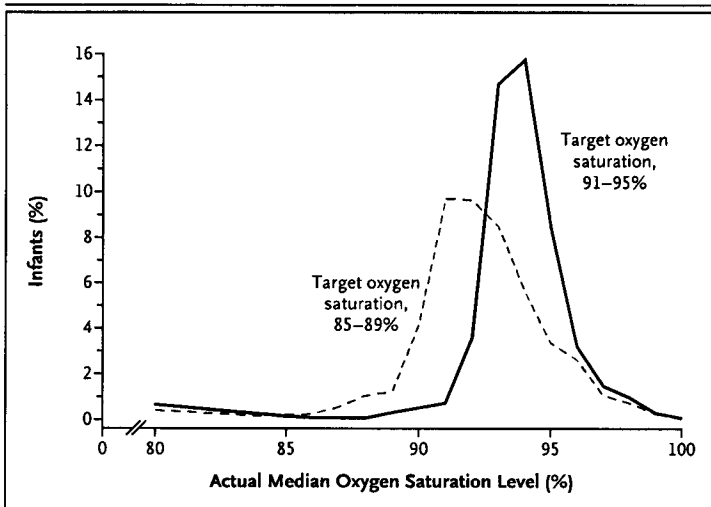


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.

The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FIO₂ concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911781.

Appendix Table 1: Cause of Death in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth Weight Infants

Category – no./total no. (%)	Lower Saturation	Higher Saturation
	Group	Group
	n/N (%)	n/N (%)
Respiratory distress syndrome	31/130 (23.8)	31/107 (29.0)
Infection	25/130 (19.2)	21/107 (19.6)
Necrotizing enterocolitis	23/130 (17.7)	14/107 (13.1)
Bronchopulmonary dysplasia	14/130 (10.8)	10/107 (9.3)
Central nervous system insult	12/130 (9.2)	9/107 (8.4)
Immaturity	7/130 (5.4)	3/107 (2.8)
Other	18/130 (13.8)	19/107 (17.8)
Causes of death did not differ		

Appendix Table 2: Effect of Retinopathy Adjudication for Low vs. High Oxygen Saturation Target Groups

Characteristic	Lower Saturation	Higher Saturation	Relative Risk for	Adjusted
	Group (N=654)	Group (N=662)	Low SpO ₂ vs. High SpO ₂ (95% CI)	P value
	n/N (%)	n/N (%)		
Severe retinopathy/death, All outcomes (non-adjudicated)	171/605 (28.3)	198/616 (32.1)	0.9 (0.76, 1.06)	0.205
Severe retinopathy among survivors, All outcomes (non-adjudicated)	41/475 (8.6)	91/509 (17.9)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed by majority rule*	171/642 (26.6)	198/656 (30.2)	0.91 (0.77, 1.07)	0.253
Severe retinopathy among survivors, Cases considered confirmed by majority rule*	41/512 (8.0)	91/549 (16.6)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed majority rule* when "unknown cases" considered to have severe retinopathy†	183/654 (28.0)	204/662 (30.8)	0.93 (0.79, 1.1)	0.412
Severe retinopathy among survivors, Cases confirmed by majority rule when "unknown cases" considered to have severe retinopathy†	53/524 (10.1)	97/555 (17.5)	0.62 (0.45, 0.84)	0.002

Relative risks are adjusted for gestational age stratification, center, and familial clustering;

*Majority rule: If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; If two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=missing.

†If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; if two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=Y.

Appendix Table 3. Other Outcomes in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth Weight Infants

Outcome	Lower Saturation Group	Higher Saturation Group	Adjusted P value [§]
Length of stay any hospital, (days) m±SE*	104.5 ± 2.0	106.4 ± 2.0	0.45
Length of stay at study hospital, (days) m±SE*	99.8 ± 2.0	103.0 ± 2.0	0.22
Duration of mechanical ventilation, (days) m±SE [†]	25.5 ± 1.1	26.9 ± 1.0	0.30
Duration of oxygen supplementation, (days) m±SE [†]	59.8 ± 1.6	67.4 ± 1.5	<0.001
Continuous positive airway pressure, (days) m±SE [†]	17.1 ± 0.6	17.0 ± 0.6	0.94
Nasal synchronized intermittent mandatory ventilation, (days) m±SE [†]	3.3 ± 0.3	3.8 ± 0.3	0.14
Alive off mechanical ventilation by day 14, (days) – no. (%)	332/644 (51.6)	326/655 (49.8)	0.86
Alive off mechanical ventilation by day 7, (days) – no. (%)	351/648 (54.2)	329/659 (49.9)	0.27
Percent of time in actual oxygen saturation range 84-96%, (%) m±SD [‡]	66.9 ± 13.9	68.0 ± 15.2	0.16 [¶]

*Among survivors to discharge, transfer or one year; maximum value is 366 days

[†]Among survivors to discharge, transfer or 120 days; maximum value is 120 days

[‡]Percent of time based only on total time on oxygen supplementation

§Adjusted for stratification factors (study center, gestational age group) as well as for familial clustering

¶Unadjusted P value

ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P<0.001$), required fewer days of mechanical ventilation ($P=0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P=0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of members of the Writing Committee and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network are listed in the Appendix. Address reprint requests to Dr. Neil N. Finer at the University of California at San Diego, 402 Dickinson St., MPF 1-140, San Diego, CA 92103-8774, or at nfiner@ucsd.edu.

This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (FiO_2) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide (PaCO_2) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a PaCO_2 below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an FiO_2 below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a PaCO_2 of less than 50 mm Hg and a pH higher than 7.30, an FiO_2 of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

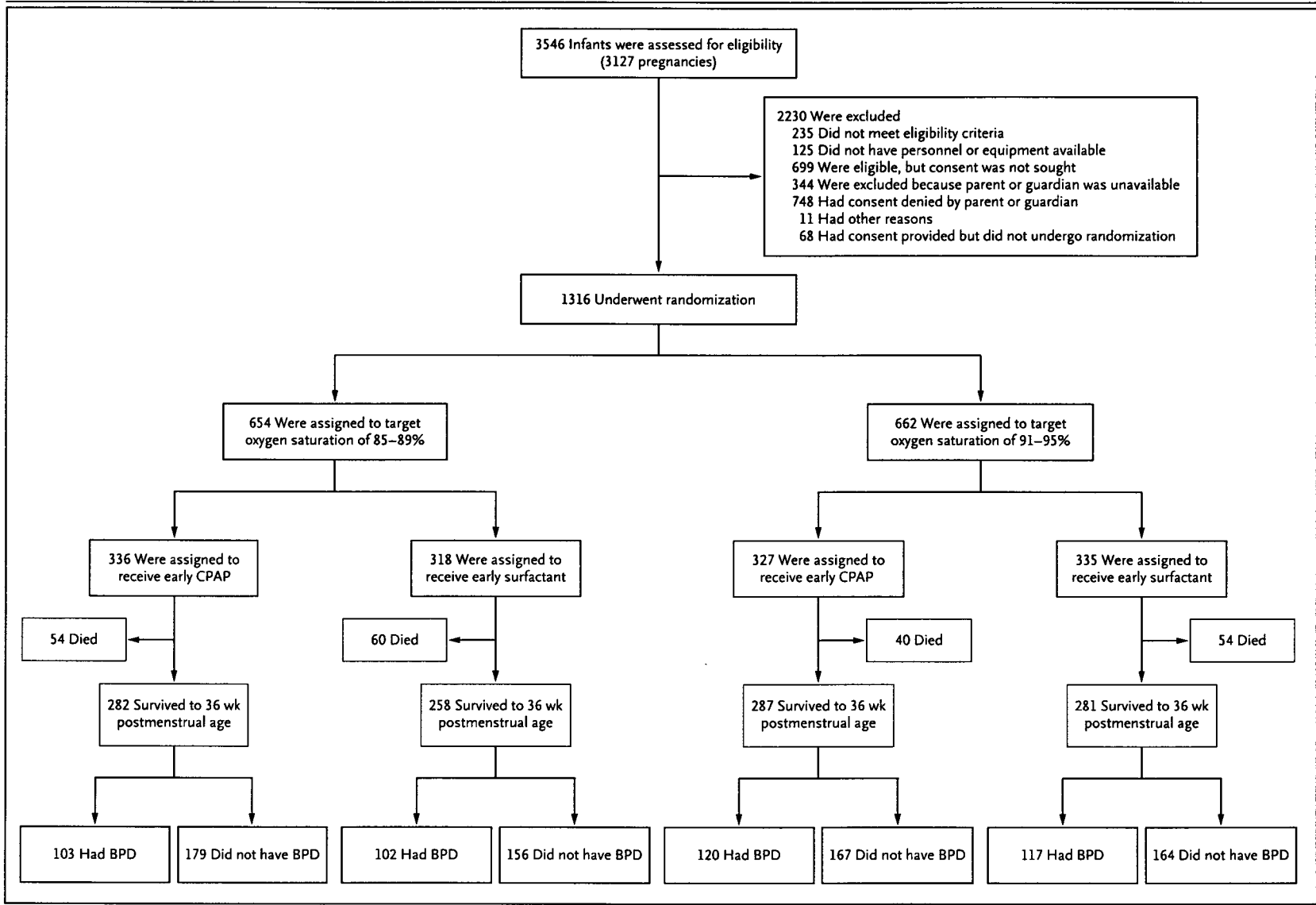


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Variable	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Adjusted P Value
	<i>no./total no. (%)</i>			
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that

Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911783.

Web Appendix Tables

Table A1. Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=421)	35.8 ± 1.5 29.5 (10, 48)	38.7 ± 1.6 33 (14, 56)	-3.0 (-7.2, 1.3)	0.17
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

Table A2. Cause of Death for 24 to 25 week stratum

Contributory Cause of Death	CPAP (N=68)	Surfactant (N=90)
Respiratory distress syndrome	13/68 (19.1)	31/90 (34.4)
Bronchopulmonary dysplasia	10/68 (14.7)	7/90 (7.8)
Infection	14/68 (20.6)	15/90 (16.7)
Necrotizing enterocolitis	10/68 (14.7)	16/90 (17.8)
Central nervous center insult	11/68 (16.2)	5/90 (5.6)
Immaturity	3/68 (4.4)	5/90 (5.6)
Other	7/68 (10.3)	11/90 (12.2)

Table A3. Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P-value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the FiO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

From the Royal Women's Hospital and the Department of Obstetrics, University of Melbourne — both in Melbourne, Australia.

This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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EDITORIAL

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From: Zeis, Jennifer
To: Higgins, Rosemary (NIH/NICHD) [E]; "Finer, Neil"
Cc: Wally_Carlo_M.D.; Martinez, Fernando; Rich, Wade
Subject: RE: Final NEJM files
Date: Wednesday, May 12, 2010 12:00:12 PM

Hi Rose,

Yes, it will.

Jen

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 12, 2010 11:57 AM
To: Zeis, Jennifer; 'Finer, Neil'
Cc: Wally_Carlo_M.D.; Martinez, Fernando; Rich, Wade
Subject: RE: Final NEJM files

Jennifer

Thank you for sending all of these. Will the Editorial be released on-line at 1 PM ET on Sunday May 16 along with the two papers?

Thanks
Rose

From: Zeis, Jennifer [mailto:jzeis@nejm.org]
Sent: Wednesday, May 12, 2010 11:34 AM
To: 'Finer, Neil'
Cc: Wally_Carlo_M.D.; Higgins, Rosemary (NIH/NICHD) [E]; Martinez, Fernando; Rich, Wade
Subject: Final NEJM files

Dear Neil,

Please find attached the final NEJM files of your article, a related article, and an editorial on the pair. The trio will be sent to the media under embargo at 10 AM EDT Thursday. Also, please find attached our standard permissions language for articles.

Many thanks, and if you have any questions, please don't hesitate to ask.

Kind regards,
Jen

Jennifer Zeis
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From: Finer, Neil [mailto:nfiner@ucsd.edu]

Sent: Tuesday, April 20, 2010 1:33 PM
To: Zeis, Jennifer
Cc: Wally_Carlo_M.D.; Higgins_Rosemary_; Martinez, Fernando; Rich, Wade
Subject: RE: Online First release schedule for NEJM 09-11783

Hello Jennifer
Thank you for this information.
I have copied Wally Carlo and Rose Higgins with this email.
My contact information is below
Regards
Neil Finer

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From: Zeis, Jennifer [mailto:jzeis@nejm.org]
Sent: Tuesday, April 20, 2010 9:39 AM
To: Finer, Neil
Subject: Online First release schedule for NEJM 09-11783

Dear Dr. Finer,

As you know, your NEJM Original Article is on an accelerated Online First release schedule to coincide with your presentation of the results at the American Thoracic Society's annual meeting. I am writing to share the details of that schedule, and to request your preferred media points of contact.

We will provide your article to reporters at 10 AM EDT Thursday, May 13. When we provide your article to the media under embargo, we will post the material on our password-protected NEJM Media Center, where only journalists who have agreed to respect our embargo may access it. I will email you this final file and any related material at that time

Your article will be embargoed until 1 PM EDT Sunday, May 16, the start of your ATS presentation on the trial. The ATS and NEJM embargoes are coordinated to lift simultaneously so you may reference your NEJM publication at the meeting, if you wish. Your paper will be published on NEJM.org as soon as the embargo lifts, and will later be published in the May 27 printed issue.

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Cc: Wally_Carlo_M.D.; Higgins, Rosemary (NIH/NICHD) [F]; Martinez, Fernando; Rich, Wade
Subject: Final NEJM files
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Hello Jennifer
Thank you for this information.
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My contact information is below
Regards
Neil Finer

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Best regards,
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ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P < 0.001$), required fewer days of mechanical ventilation ($P = 0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P = 0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a previous study reported in the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (FiO_2) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an FiO_2 below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 breaths per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an FiO_2 of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 breaths per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.

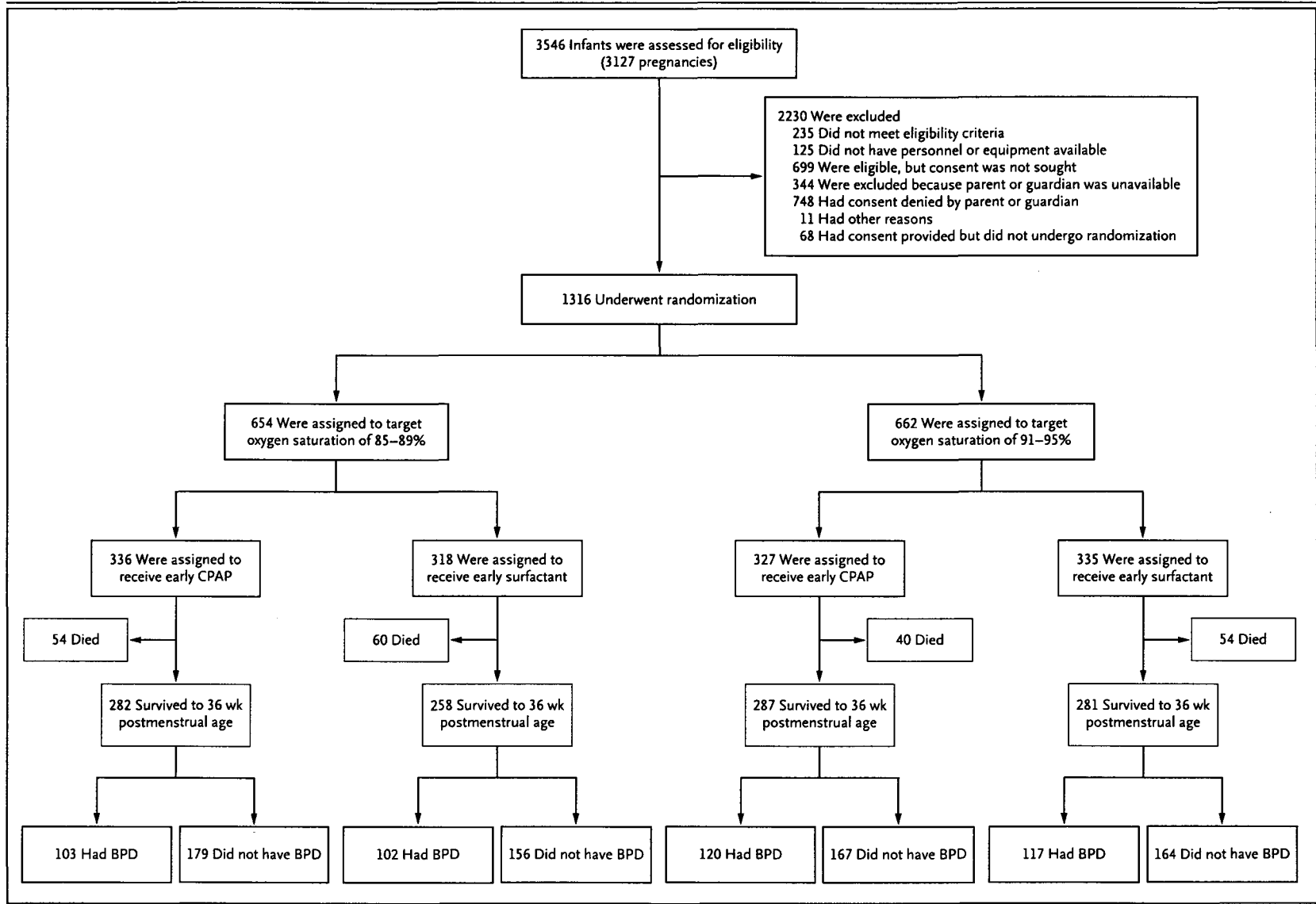


Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix, available with the full text of this article at NEJM.org]); in contrast, there was no significant between-group difference in the rate of

Table 2. Apgar Scores of Newborns and Interventions in the Delivery Room and NICU.*

Variable	CPAP (N = 663) no./total no. (%)	Surfactant (N = 653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

death during hospitalization or at 36 weeks among the infants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively; rate of death at 36 weeks: 9.8% and 8.6%, respectively) (see Tables A1 and A3 in the Supplementary Appendix).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that

Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744) from the National Institutes of Health.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010. DOI: 10.1056/NEJMoa0911783.

Web Appendix Tables

Table A1. Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted	35.8 ± 1.5	38.7 ± 1.6	-3.0 (-7.2, 1.3)	0.17
Mean±StdErr, Unadjusted Median (IQR) (N=421)	29.5 (10, 48)	33 (14, 56)		
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

Table A2. Cause of Death for 24 to 25 week stratum

Contributory Cause of Death	CPAP (N=68)	Surfactant (N=90)
Respiratory distress syndrome	13/68 (19.1)	31/90 (34.4)
Bronchopulmonary dysplasia	10/68 (14.7)	7/90 (7.8)
Infection	14/68 (20.6)	15/90 (16.7)
Necrotizing enterocolitis	10/68 (14.7)	16/90 (17.8)
Central nervous center insult	11/68 (16.2)	5/90 (5.6)
Immaturity	3/68 (4.4)	5/90 (5.6)
Other	7/68 (10.3)	11/90 (12.2)

Table A3. Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P-value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

† Among survivors to discharge, transfer or 120 days; maximum value is 120 days

ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD
Neonatal Research Network*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of the authors and other investigators in the Surfactant, Positive Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development are listed in the Appendix. Address reprint requests to Dr. Waldemar A. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@pediatrics.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FIO₂) to no more than 0.50, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that levels of oxygen saturation previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor levels of oxygen saturation and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual levels of oxygen saturation achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, a reading of 90% corresponded to actual levels of oxygen saturation of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate levels of oxygen saturation in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (non-skewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of levels of oxygen saturation with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36 weeks of postmenstrual age or until the in-

fant was breathing ambient air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Data on oxygen saturation were electronically sampled every 10 seconds and downloaded by the data center. Readings of levels of oxygen saturation that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity or plus disease with stage 3 retinopathy of

prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 47% in the Neonatal Research Network for the year

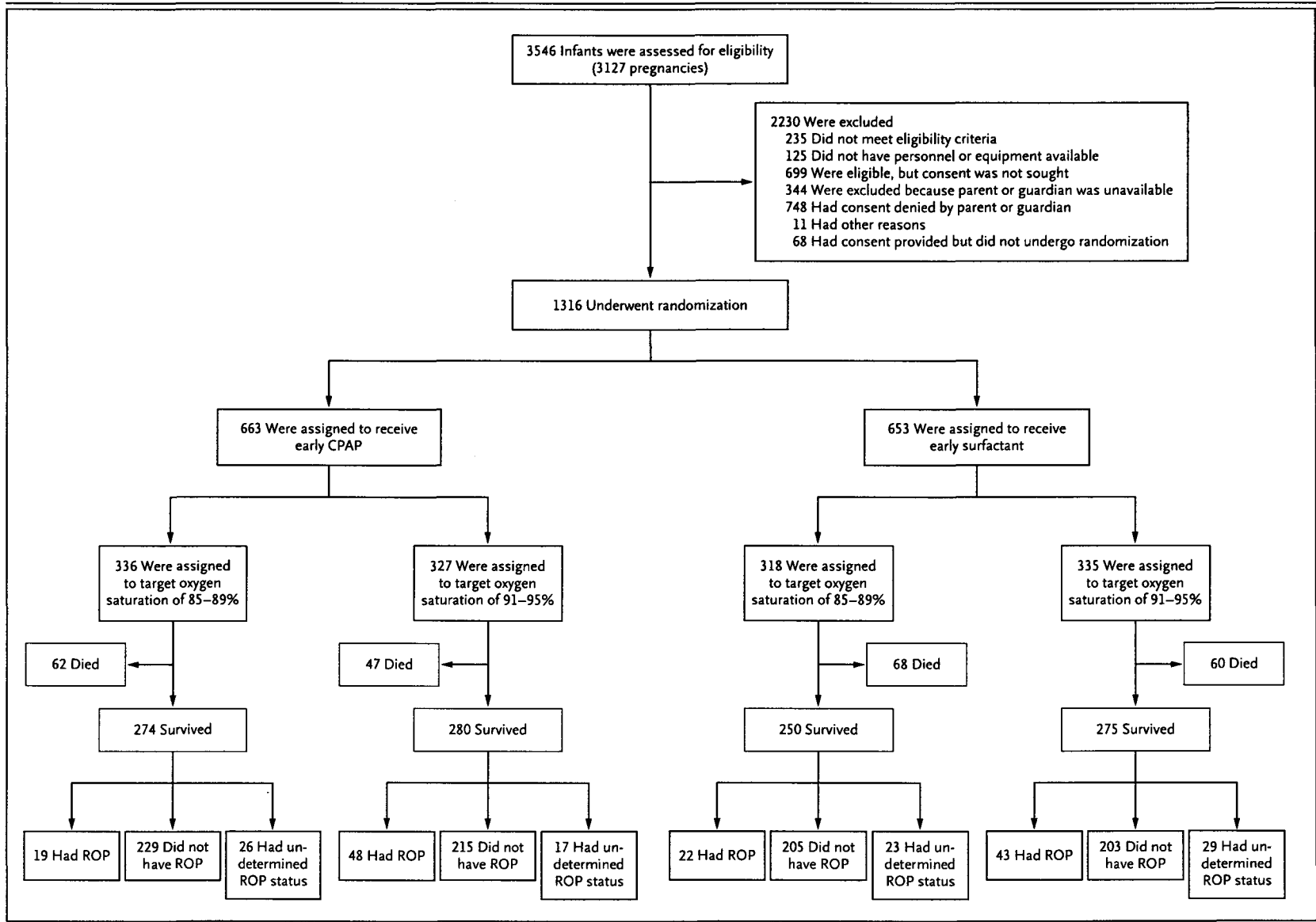
Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the data on oxygen saturation to evaluate compliance with the protocol. The Lan-DeMets spend-



Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

ing functions with Pocock and O'Brien-Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of levels of oxygen saturation often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing ambient air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resump-

tion of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the level of oxygen saturation and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

full text of this article at NEJM.org). Similar results were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$).

The rate of severe retinopathy among survivors who were discharged or transferred to another facility or who reached the age of 1 year was lower in the lower-oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$; number needed to treat, 11). Although

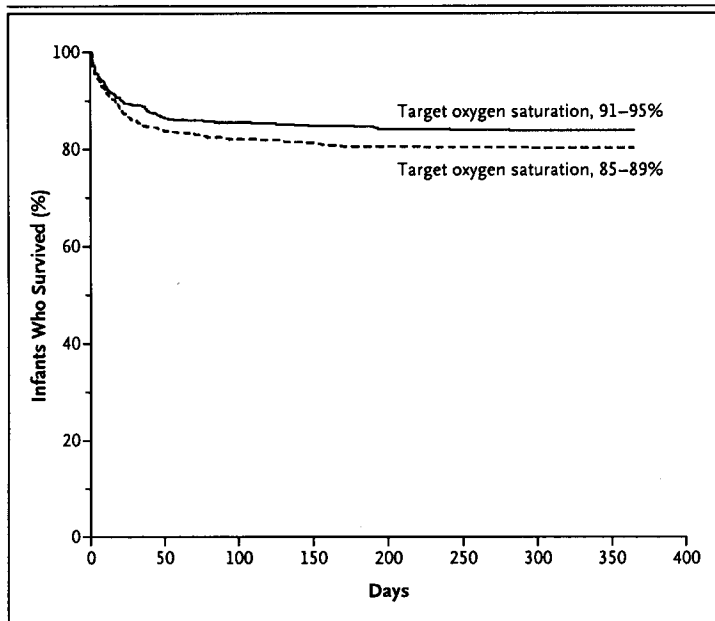


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.

Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

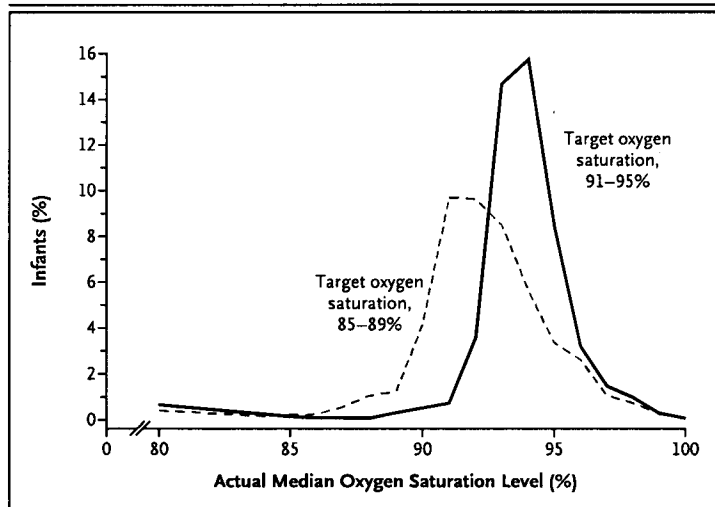


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.

The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% level of oxygen saturation shown includes all values at or below 80%.

opathy or surgical intervention for retinopathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological test of oxygen saturation at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median level of oxygen saturation in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual levels of oxygen saturation between the two treatment groups. Previous trials of targeting of levels of oxygen saturation have shown similar difficulties in maintaining levels of oxygen saturation within a narrow target range.^{18,22} Longer follow-up will be required to determine

use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of levels of oxygen saturation, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO_2 concentration usually to less than

0.50, at a time before the continuous monitoring of arterial oxygen saturation was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous monitoring of oxygen saturation. Like the meta-analysis²⁴ and most non-randomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting levels of oxygen saturation in the low range for preterm infants, since it may lead to increased mortality.

Supported by grants (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, cofunding from the National Heart, Lung, and Blood Institute, and grants (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, and UL1 RR25744) from the National Institutes of Health.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010. DOI: 10.1056/NEJMoa0911781.

Appendix Table 1: Cause of Death in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low Birth Weight Infants

Category – no./total no. (%)	Lower Saturation	Higher Saturation
	Group	Group
	n/N (%)	n/N (%)
Respiratory distress syndrome	31/130 (23.8)	31/107 (29.0)
Infection	25/130 (19.2)	21/107 (19.6)
Necrotizing enterocolitis	23/130 (17.7)	14/107 (13.1)
Bronchopulmonary dysplasia	14/130 (10.8)	10/107 (9.3)
Central nervous system insult	12/130 (9.2)	9/107 (8.4)
Immaturity	7/130 (5.4)	3/107 (2.8)
Other	18/130 (13.8)	19/107 (17.8)
Causes of death did not differ		

Appendix Table 2: Effect of Retinopathy Adjudication for Low vs. High Oxygen Saturation Target Groups

Characteristic	Lower Saturation	Higher Saturation	Relative Risk for	Adjusted
	Group (N=654)	Group (N=662)	Low SpO ₂ vs. High SpO ₂ (95% CI)	P value
	n/N (%)	n/N (%)		
Severe retinopathy/death, All outcomes (non-adjudicated)	171/605 (28.3)	198/616 (32.1)	0.9 (0.76, 1.06)	0.205
Severe retinopathy among survivors, All outcomes (non-adjudicated)	41/475 (8.6)	91/509 (17.9)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed by majority rule*	171/642 (26.6)	198/656 (30.2)	0.91 (0.77, 1.07)	0.253
Severe retinopathy among survivors, Cases considered confirmed by majority rule*	41/512 (8.0)	91/549 (16.6)	0.52 (0.37, 0.73)	<0.001
Severe retinopathy/death, Cases considered confirmed majority rule* when "unknown cases" considered to have severe retinopathy†	183/654 (28.0)	204/662 (30.8)	0.93 (0.79, 1.1)	0.412
Severe retinopathy among survivors, Cases confirmed by majority rule when "unknown cases" considered to have severe retinopathy†	53/524 (10.1)	97/555 (17.5)	0.62 (0.45, 0.84)	0.002

Relative risks are adjusted for gestational age stratification, center, and familial clustering;

*Majority rule: If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; If two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=missing.

†If two reviewers determined that the infant 'Probably never had retinopathy that met criteria for severe retinopathy intervention (laser/cryotherapy) in either eye' then retinopathy=N; if two reviewers determined that 'There is no way to know if severe retinopathy criteria may have been met' then severe retinopathy=Y.

Appendix Table 3. Other Outcomes in a Randomized Trial of Lower versus Higher Oxygen Saturation Targets in Extremely Low

Birth Weight Infants

Outcome	Lower Saturation Group	Higher Saturation Group	Adjusted P value [§]
Length of stay any hospital, (days) m±SE*	104.5 ± 2.0	106.4 ± 2.0	0.45
Length of stay at study hospital, (days) m±SE*	99.8 ± 2.0	103.0 ± 2.0	0.22
Duration of mechanical ventilation, (days) m±SE [†]	25.5 ± 1.1	26.9 ± 1.0	0.30
Duration of oxygen supplementation, (days) m±SE [†]	59.8 ± 1.6	67.4 ± 1.5	<0.001
Continuous positive airway pressure, (days) m±SE [†]	17.1 ± 0.6	17.0 ± 0.6	0.94
Nasal synchronized intermittent mandatory ventilation, (days) m±SE [†]	3.3 ± 0.3	3.8 ± 0.3	0.14
Alive off mechanical ventilation by day 14, (days) – no. (%)	332/644 (51.6)	326/655 (49.8)	0.86
Alive off mechanical ventilation by day 7, (days) – no. (%)	351/648 (54.2)	329/659 (49.9)	0.27
Percent of time in actual oxygen saturation range 84-96%, (%) m±SD [‡]	66.9 ± 13.9	68.0 ± 15.2	0.16 [¶]

*Among survivors to discharge, transfer or one year; maximum value is 366 days

[†]Among survivors to discharge, transfer or 120 days; maximum value is 120 days

[‡]Percent of time based only on total time on oxygen supplementation

§Adjusted for stratification factors (study center, gestational age group) as well as for familial clustering

¶Unadjusted P value

EDITORIAL



CPAP and Low Oxygen Saturation for Very Preterm Babies?

Colin J. Morley, M.D.

The survival rate among extremely preterm babies — those born at 24 to 27 weeks of gestation — is about 75%, and there is a high prevalence of neurodevelopmental problems. Reducing the rates of complications and death among these infants is a key research area. Traditionally, extremely preterm babies have been treated with intubation and ventilation soon after birth. However, these interventions may contribute to lung injury. Many infants breathe adequately but not normally at birth, and some can be assisted with the less invasive strategy of nasal continuous positive airway pressure (CPAP) and receive ventilation and surfactant only if this strategy fails.^{1,2} Oxygen therapy is very toxic for preterm babies, and maintaining even slightly high arterial levels contributes to retinopathy of prematurity and increases the duration of oxygen treatment.³ Unfortunately, an oxygen saturation (SpO₂) range that reduces retinopathy of prematurity optimally but does not increase the rates of death or neurodevelopmental problems has not been accurately defined.

The results of the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a randomized, 2-by-2 factorial trial in which 1316 babies who were born between 24 weeks 0 days and 27 weeks 6 days of gestation were enrolled, are reported in this issue of the *Journal*.^{4,5} In this trial, early treatment with CPAP was compared with immediate intubation followed by surfactant, and a target oxygen saturation range of 85 to 89% was compared with a target range of 91 to 95%.

In one part of the trial,⁵ babies were randomly assigned, before birth, to either intubation in the delivery room and surfactant administration within an hour or nasal CPAP started in the delivery room. Babies who were randomly assigned

to CPAP could be intubated in the delivery room, for the purpose of resuscitation, or later, if predefined criteria were met. Extubation criteria were also predefined; the criteria for threshold levels of the partial pressure of arterial carbon dioxide (PaCO₂), pH, the fraction of inspired oxygen (FiO₂), and SpO₂ were more stringent for the intubation group than for the CPAP group. The rates of the primary outcome of death or bronchopulmonary dysplasia⁶ did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; P=0.30). The CPAP group, as compared with the surfactant group, less frequently required intubation in the delivery room (34.4% vs. 93.4%) or postnatal corticosteroids for the treatment of bronchopulmonary dysplasia (7.2% vs. 13.2%) (P<0.001 for both comparisons), and required ventilation for an average of 3 days less (P=0.03). There were no significant differences between the two groups in the incidences of death or other major outcomes before discharge from the hospital. These results are similar to those of the Continuous Positive Airway Pressure or Intubation at Birth trial (COIN; Australian New Zealand Clinical Trials Registry number, 12606000258550),² in which 610 babies who were born at 25 to 28 weeks of gestation were randomly assigned to CPAP or intubation and ventilation at 5 minutes after birth.

Some limitations of the present trial should be noted. Randomization was performed before delivery (i.e., before it was known whether babies would breathe or have respiratory distress); as a result, some of the infants in the CPAP group were intubated immediately after birth and did not receive CPAP. The median duration of ventilation for both groups was 3 to 4 weeks, which was much longer than the 3 to 4 days in the COIN tri-

al,² and suggests that the extubation criteria in this trial were more stringent than were those in the COIN trial. In the COIN trial,² pneumothorax occurred in 3.0% of the infants in the CPAP group and in 9.1% of the infants in the ventilation group. In the SUPPORT trial, they occurred in 6.8% of the infants in the CPAP group and in 7.4% of the infants in the ventilation group, a finding that suggests that early CPAP is not associated with pneumothorax.

In the other part of SUPPORT,⁴ the babies were randomly assigned to a target range for peripheral oxygen saturation of 85 to 89% or 91 to 95%. Staff members were unaware of the true levels because the oximeters had been altered to read 3% above or 3% below the true reading, so that they displayed a range of 88 to 92% for both ranges. The unmasked trial data showed that the distribution of oxygen saturation levels was within or above the target range in the higher-oxygen-saturation group, but in the lower-oxygen-saturation group, it was about 90 to 95% (i.e., above the target range). The difference in oxygen saturation levels between the groups was about 3 percentage points instead of the 6 percentage points that had been planned. Therefore, this study actually compared saturation levels of about 89 to 97% with saturation levels of 91 to 97%; the results should be ascribed to these higher ranges. There is evidence that nurses tend to keep a baby's oxygen saturation level toward the higher end of the range,⁷ which may account for the shift of both groups toward higher saturation levels than those targeted.

There was no significant difference between the oxygen-saturation groups in the primary outcome of severe retinopathy of prematurity or death before discharge. However, even with the relatively modest difference in oxygen saturation levels between the groups, the rate of severe retinopathy of prematurity was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group (8.6% vs. 17.9%, $P < 0.001$).

Moderate-to-severe bronchopulmonary dysplasia is defined as the need for supplemental oxygen in a very preterm infant at 36 weeks of postmenstrual age.⁸ This trial also used a physiological definition of bronchopulmonary dysplasia, which calls for the FiO_2 to be reduced at 36 weeks in order to determine whether supplemental oxygen is really required.⁶ As in previous studies,⁹ the rate of needed treatment with supplemental oxy-

gen at 36 weeks among survivors was lower in the lower-oxygen-saturation group than in the higher-oxygen-saturation group ($P = 0.002$). When the physiological definition of bronchopulmonary dysplasia was used, the rate of oxygen use at 36 weeks was not altered in the lower-oxygen-saturation group but it was reduced in the higher-oxygen-saturation group, with the result that the difference between the groups was no longer significant. The rate of the composite of death or bronchopulmonary dysplasia (according to either definition) by 36 weeks did not differ significantly between the groups.

There was weak evidence¹⁰ of an increased rate of death before discharge in the lower-oxygen-saturation group ($P = 0.04$). An association between lower oxygen-saturation targets and increased mortality has been reported previously in some¹¹ but not other^{3,12} nonrandomized studies and was not observed in a previous randomized trial.⁹ This is a most important outcome, but caution is warranted in interpreting this result. Additional research is needed to clarify this finding. There were no significant differences between the groups in short-term outcomes that have been associated with relative ischemia.

How do the results of this trial help neonatologists? They show that starting CPAP at birth in very preterm babies, even if it fails in some, has important benefits and no serious side effects. Predicting which babies will not have an adequate response to treatment with CPAP and should therefore receive early ventilation and surfactant should be a future goal. Targeting oxygen saturation levels is difficult, and a recommended oxygen saturation range that is effective yet safe remains elusive. A lower oxygen saturation level significantly reduces the incidence of severe retinopathy of prematurity but may increase the rate of death. Long-term follow-up is vital to determine whether either intervention was associated with neurodevelopmental problems.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1004342) was published on May 16, 2010, at NEJM.org.

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Here they are – thanks for all your help!!!
Rose

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ORIGINAL ARTICLE

Target Ranges of Oxygen Saturation in Extremely Preterm Infants

The NICHD Neonatal Research Network and the SUPPORT Study Group*

ABSTRACT

BACKGROUND

Previous studies have suggested that the incidence of retinopathy is lower in preterm infants with exposure to reduced levels of oxygenation than in those exposed to higher levels of oxygenation. However, it is unclear what range of oxygen saturation is appropriate to minimize retinopathy without increasing adverse outcomes.

METHODS

We performed a randomized trial with a 2-by-2 factorial design to compare target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. The primary outcome was a composite of severe retinopathy of prematurity (defined as the presence of threshold retinopathy, the need for surgical ophthalmologic intervention, or the use of bevacizumab), death before discharge from the hospital, or both. All infants were also randomly assigned to continuous positive airway pressure or intubation and surfactant.

RESULTS

The rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; $P=0.21$). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; relative risk, 1.27; 95% CI, 1.01 to 1.60; $P=0.04$), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; $P<0.001$). There were no significant differences in the rates of other adverse events.

CONCLUSIONS

A lower target range of oxygenation (85 to 89%), as compared with a higher range (91 to 95%), did not significantly decrease the composite outcome of severe retinopathy or death, but it resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern, since a lower target range of oxygen saturation is increasingly being advocated to prevent retinopathy of prematurity. (ClinicalTrials.gov number, NCT00233324.)

*The authors are listed in the Appendix. The affiliations of members of the Writing Committee and the other investigators in the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the Surfactant, Positive Airway Pressure, and Pulse Oximetry Randomized Trial (SUPPORT) Study Group are listed in the Appendix. Address reprint requests to Dr. Carlo at the University of Alabama at Birmingham, 176F Suite 9380, 619 S. 19th St., Birmingham, AL 35294-7335, or at wcarlo@peds.uab.edu.

This article (10.1056/NEJMoa0911781) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.

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RETINOPATHY OF PREMATURITY IS AN important cause of blindness and other visual disabilities in preterm infants. The incidence of retinopathy of prematurity was increased with exposure to unrestricted oxygen supplementation in preterm infants in randomized, controlled trials performed in the 1950s.¹ In the 1960s, this increase resulted in the practice of restricting the fraction of inspired oxygen (FiO₂) to no more than 50%, which was estimated to result in an excess of 16 deaths per case of blindness prevented.² More recent data suggest that oxygen-saturation levels previously thought to be at the upper end of the normal range may increase the risk of retinopathy of prematurity as compared with levels at the lower end of the normal range.³⁻⁵ Oxygen toxicity may also increase the risk of death,^{6,7} bronchopulmonary dysplasia,⁸⁻¹⁰ periventricular leukomalacia,¹¹ cerebral palsy,¹² and other conditions. Although a multicenter observational study did not show a significant association between higher values for the partial pressure of arterial oxygen and retinopathy, a single-center cohort study involving transcutaneous oxygen monitoring provided support for an association between an increased risk of retinopathy¹³ and exposure to arterial oxygen levels of 80 mm Hg or more.¹⁴

Pulse oximetry allows clinicians to continuously monitor oxygen-saturation levels and to target levels in a defined range. Associations between lower target levels of oxygen saturation and a lower incidence of retinopathy have been reported.¹⁻⁵ In a survey of 144 neonatal intensive care units (NICUs), the rate of retinal ablation surgery among very-low-birth-weight infants was increased among infants cared for in NICUs that used higher maximum target levels of oxygen saturation, as compared with infants in NICUs that used lower target levels. The rate of retinal ablation surgery was 3.3% in NICUs using target levels of 92% or higher and 1.4% in NICUs using target levels of less than 92%; the rate was 5.6% in NICUs using target levels of 98% or higher and 3.1% in NICUs using target levels of less than 98%.³ In a retrospective study comparing outcomes at five NICUs, the incidence of severe retinopathy requiring ablation therapy was 27% in NICUs where the target saturation level was 88 to 98% and only 6% in NICUs where the target level was 70 to 90%.³ Rates of death and cerebral

palsy did not differ significantly among these NICUs. In three studies with a before-and-after design, the implementation of a policy of target levels of oxygen saturation of approximately 83 to 95% was associated with a substantial reduction in the incidence of retinopathy, as compared with the period before implementation of the policy; however, the actual oxygen-saturation levels achieved, mortality, and neurodevelopmental outcomes were not reported.^{4,15,16} Although data from these studies suggest that maintenance of oxygenation at ranges lower than those previously used may decrease the incidence of retinopathy of prematurity, the safety of low target levels of oxygen saturation remains a concern.

We conducted the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), a controlled, multicenter trial with a 2-by-2 factorial design, to compare two target levels of oxygen saturation and two ventilation approaches (continuous positive airway pressure [CPAP] initiated in the delivery room with a protocol-driven strategy of limited ventilation vs. intratracheal administration of surfactant with a protocol-driven strategy of conventional ventilation). The oxygen-saturation component of the trial tested the hypothesis that a lower target range of oxygen saturation (85 to 89%), as compared with a higher target range (91 to 95%), would reduce the incidence of the composite outcome of severe retinopathy of prematurity or death among infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation. The ventilation part of this factorial-design trial, which was used to control the ventilation approach and test other hypotheses, is reported elsewhere in this issue of the *Journal*.¹⁷

METHODS

STUDY DESIGN

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the institutional review board at each participating site and by RTI International, which is the independent data coordinating center for the Neonatal Research Network. Data collected at the study sites were transmitted to RTI International, which stored, managed, and analyzed the data for this

study. Written informed consent was obtained from the parent or guardian of each child before delivery.

PATIENTS

Infants who were born between 24 weeks 0 days of gestation and 27 weeks 6 days of gestation for whom a decision had been made to provide full resuscitation were eligible for enrollment at birth. Infants born in other hospitals and those known to have major congenital anomalies were excluded.

ENROLLMENT AND TREATMENT

Infants were enrolled from February 2005 through February 2009. Permuted-block randomization was used, with stratification according to study center and gestational age (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days). Using sealed, opaque envelopes, we randomly assigned infants before birth to a target range of oxygen saturation of 85 to 89% (the lower-oxygen-saturation group) or 91 to 95% (the higher-oxygen-saturation group). Infants who were part of multiple births were randomly assigned to the same group.

Blinding was maintained with the use of electronically altered pulse oximeters (Masimo Radical Pulse Oximeter) that showed saturation levels of 88 to 92% for both targets of oxygen saturation, with a maximum variation of 3%. For example, an oxygen-saturation reading of 90% corresponded to actual oxygen-saturation levels of 87% in the group assigned to lower oxygen saturation (85 to 89%) and 93% in the group assigned to higher oxygen saturation (91 to 95%). A previous trial used a fixed 3% absolute oxygen-saturation variation throughout the entire range of saturation levels to keep caregivers unaware of study-group assignments and to separate oxygen-saturation levels in preterm infants,¹⁸ but the algorithm used in the current trial differed, since the oxygen-saturation reading gradually changed and reverted to actual (nonskewed) values when it was less than 84% or higher than 96% in both treatment groups. Limits of 85% and 95% that would trigger an alarm in the delivery system were suggested, but they could be changed for individual patients.

Targeting of oxygen-saturation levels with altered pulse oximetry was initiated within the first 2 hours after birth and was continued until 36

weeks of postmenstrual age or until the infant was breathing room air and did not require ventilator support or CPAP for more than 72 hours, whichever occurred first. Infants who were weaned to room air but who subsequently received oxygen supplementation before 36 weeks of postmenstrual age were placed back on the assigned study pulse oximeter. The target ranges were kept unchanged from birth until 36 weeks of postmenstrual age. Adjustments in supplemental oxygen to maintain the target level of oxygen saturation between 88 and 92% were performed by the clinical staff rather than the research staff.

Oxygen-saturation data were electronically sampled every 10 seconds and downloaded by the data center. Oxygen-saturation readings that were pooled (i.e., not separated according to treatment group) were provided quarterly to each center for feedback on compliance. Actual data on oxygen saturation were not provided to the clinicians or researchers but are used exclusively in this article. For the ventilation part of this trial with a 2-by-2 factorial design, participants were randomly assigned to CPAP with a protocol-driven limited ventilation strategy or to prophylactic early administration of surfactant with a protocol-driven conventional ventilation strategy.¹⁷

ASSESSMENTS

Research nurses recorded all data using standardized definitions included in the trial's manual of operations. Data collection, excluding examinations to detect retinopathy of prematurity, was completed at discharge. All surviving infants were followed by ophthalmologists trained in the diagnosis of retinopathy of prematurity. Examinations began by 33 weeks of postmenstrual age and continued until the study outcome was reached or resolution occurred. Resolution was defined as fully vascularized retinas or immature vessels in zone 3 for two consecutive examinations in each eye. Threshold retinopathy of prematurity (called "new type 1 threshold" by the Early Treatment of Retinopathy Cooperative Group^{19,20}) was diagnosed if any of the following findings were present: in zone 1, stage 3 retinopathy of prematurity, even without plus disease (i.e., two or more quadrants of dilated veins and tortuous arteries in the posterior pole), or plus disease with any stage of retinopathy of prematurity; in zone 2, plus disease with stage 2 retinopathy of prematurity.

rity or plus disease with stage 3 retinopathy of prematurity. Surgical ophthalmologic intervention was recorded if any of the following occurred: laser therapy, cryotherapy, both laser therapy and cryotherapy, scleral buckling, or vitrectomy. The primary outcome was death before discharge or severe retinopathy as defined by threshold retinopathy, ophthalmologic surgery, or the use of bevacizumab treatment for retinopathy. The original study protocol specified a primary outcome of death before 36 weeks of postmenstrual age, but this was changed to death before discharge before any data analyses were performed. All other outcomes reported were prespecified, including assessment of the need for oxygen at 36 weeks of postmenstrual age²¹ and safety outcomes.

STATISTICAL ANALYSIS

The analysis for the oxygen-saturation part of this factorial trial compared the percentage of infants in each treatment group in whom the primary outcome of severe retinopathy or death occurred. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors. We performed a post hoc survival analysis with the use of a Cox proportional-hazards model to compare mortality in the two oxygen-saturation groups, assuming that there were no subsequent deaths among the infants who were discharged. In the analysis of all outcomes, the results were adjusted, as prespecified, for stratification according to study center and gestational age, as well as for familial clustering due to random assignment of infants who were part of multiple births to the same treatment group. To compare the actual oxygen-saturation values in the two treatment groups, the median oxygen-saturation value during oxygen supplementation was determined for each infant. Those values were plotted according to treatment group, and the medians of the resulting distributions were compared with the use of a rank-sum test.

An absolute between-group difference of 10 percentage points in the rate of the composite primary outcome was considered clinically important. The sample-size calculations were based on the rate of death or threshold retinopathy of 50%

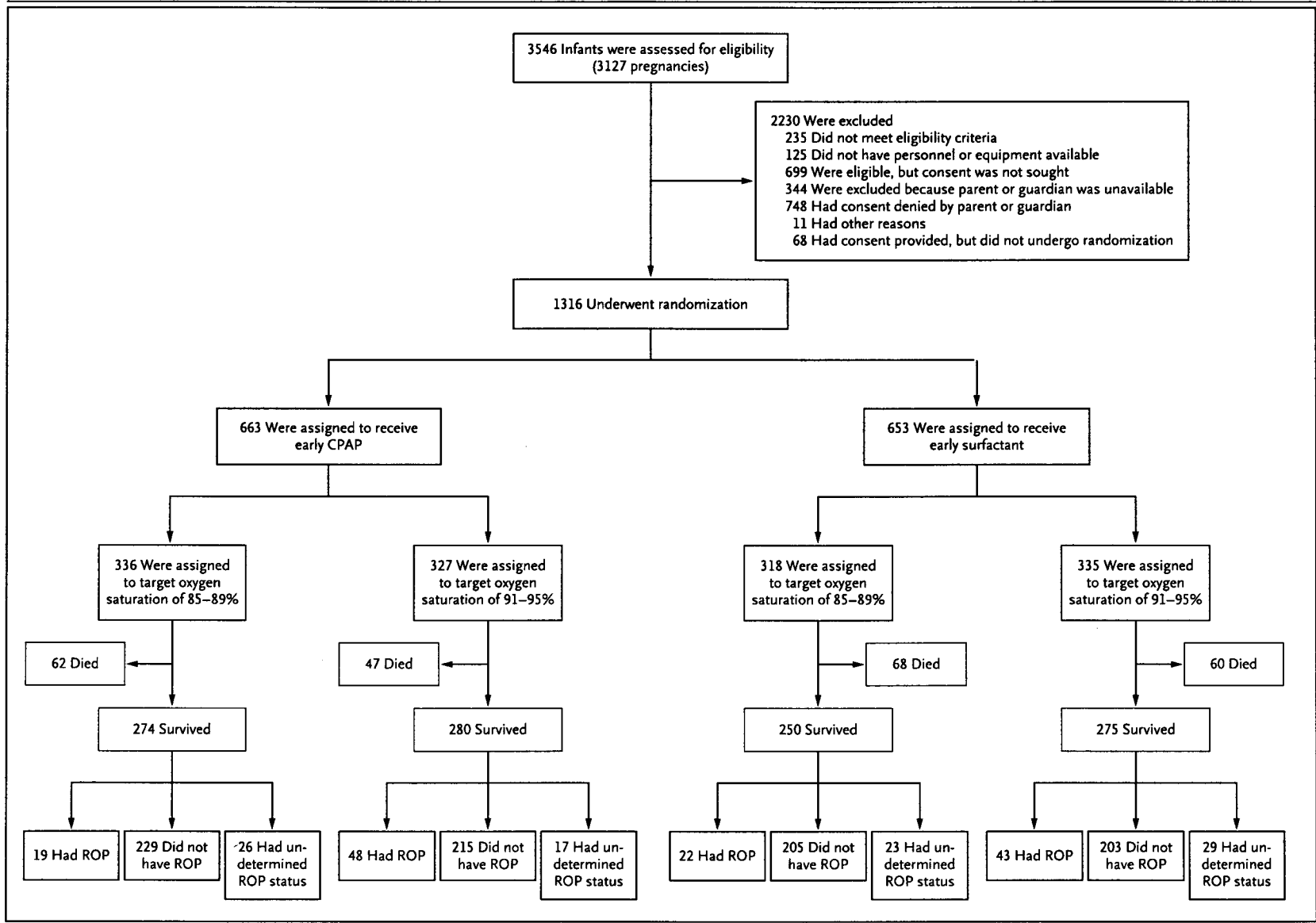
Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers shown exclude infants of women who were screened during pregnancy but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. The outcome of severe retinopathy of prematurity (ROP) could not be determined in some infants because of loss to follow-up. CPAP denotes continuous positive airway pressure.

in the Neonatal Research Network for the year 2000. We increased the sample size by a factor of 1.12 to allow for infants who were part of multiple births to be randomly assigned to the same treatment (since this introduced a clustering effect into the design), and we increased the sample size by an additional 17% to adjust for attrition after hospital discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. The study was not powered to detect an interaction effect between the two factorial parts of the study.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. All analyses were conducted at the data center. Two-sided P values of less than 0.05 were considered to indicate statistical significance. Analyses of secondary outcomes did not include adjustment for multiple comparisons; however, for the 46 planned analyses of secondary outcomes according to treatment group, we would expect no more than three tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for predefined outcomes. Although these tests were not adjusted for multiple comparisons, we would expect no more than two tests per stratum to have P values of less than 0.05 on the basis of chance alone.

An independent data and safety monitoring committee appointed by the director of the National Institute of Child Health and Human Development reviewed the primary outcomes, adverse events, and other interim results at approximately 25%, 50%, and 75% of planned enrollment. In addition, the data and safety monitoring committee, at the request of the investigators, evaluated the oxygen-saturation data to evaluate compliance



Characteristic	Lower Oxygen Saturation (N=654)	Higher Oxygen Saturation (N=662)
Birth weight — g	836±193	825±193
Gestational age — wk	26±1	26±1
Male sex — no./total no. (%)	341/654 (52.1)	371/662 (56.0)
Race or ethnic group — no./total no. (%)†		
Non-Hispanic white	242/654 (37.0)	279/662 (42.1)
Non-Hispanic black	257/654 (39.3)	232/662 (35.0)
Hispanic	132/654 (20.2)	127/662 (19.2)
Other or unknown	23/654 (3.5)	24/662 (3.6)
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	633/654 (96.8)	632/661 (95.6)
Full course	477/651 (73.3)	462/658 (70.2)
Apgar score <3 at 5 min — no./total no. (%)	34/654 (5.2)	24/662 (3.6)
Surfactant treatment — no./total no. (%)	531/653 (81.3)	558/660 (84.5)
Multiple birth — no./total no. (%)	161/654 (24.6)	176/662 (26.6)

* Plus-minus values are means ±SD. P>0.05 for all comparisons.

† Race or ethnic group was reported by the mother or guardian of each child.

with the protocol. The Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to develop stopping rules for interim safety and efficacy monitoring, respectively. In the final analysis, the nominal level of significance was 0.05. The monitored safety outcomes included death, pneumothorax, intraventricular hemorrhage, and a combination of any of these events.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

We enrolled 1316 infants in the study (Fig. 1). When 247 infants had been enrolled, enrollment was temporarily suspended on the basis of the recommendation of the data and safety monitoring committee and the decision of the director of the National Institute of Child Health and Human Development because of concern that readings of oxygen-saturation levels often exceeded the target levels. Separation of the oximetry data according to whether patients were breathing room air or receiving oxygen supplementation addressed this concern, because infants who did not require supplemental oxygen accounted for a large proportion of the high saturation levels. Resumption

of enrollment was approved. The baseline characteristics of the two treatment groups were similar (Table 1).

PRIMARY OUTCOME

The rate of the composite primary outcome, severe retinopathy or death before discharge, did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3 and 32.1%, respectively; relative risk with lower oxygen saturation, 0.90; 95% confidence interval [CI], 0.76 to 1.06; P=0.21) (Table 2). Although the trial was not powered to detect an interaction between the oxygen-saturation level and the ventilation intervention, we prospectively planned to evaluate this interaction, and no significant interaction was found (P=0.57). Death before discharge occurred in 130 of 654 infants in the lower-oxygen-saturation group (19.9%) as compared with 107 of 662 infants in the higher-oxygen-saturation group (16.2%) (relative risk with lower oxygen saturation, 1.27; 95% CI, 1.01 to 1.60; P=0.04; number needed to harm, 27). The distribution of the major causes of death did not differ significantly between the two groups (see Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Similar re-

Table 2. Major Outcomes.*

Outcome	Lower Oxygen Saturation (N = 654)	Higher Oxygen Saturation (N = 662)	Adjusted Relative Risk (95% CI)
	<i>no./total no. (%)</i>		
Severe retinopathy of prematurity or death before discharge	171/605 (28.3)	198/616 (32.1)	0.90 (0.76–1.06)
Severe retinopathy of prematurity	41/475 (8.6)	91/509 (17.9)	0.52 (0.37–0.73)
Death			
Before discharge	130/654 (19.9)	107/662 (16.2)	1.27 (1.01–1.60)
By 36 wk postmenstrual age	114/654 (17.4)	94/662 (14.2)	1.27 (0.99–1.63)
BPD, defined by use of supplemental oxygen, at 36 wk	203/540 (37.6)	265/568 (46.7)	0.82 (0.72–0.93)
BPD, defined by use of supplemental oxygen, or death by 36 wk	317/654 (48.5)	359/662 (54.2)	0.91 (0.83–1.01)
BPD, physiological definition, at 36 wk†	205/540 (38.0)	237/568 (41.7)	0.92 (0.81–1.05)
BPD, physiological definition, or death by 36 wk†	319/654 (48.8)	331/662 (50.0)	0.99 (0.90–1.10)
Intraventricular hemorrhage, grade 3 or 4‡	83/630 (13.2)	81/640 (12.7)	1.06 (0.80–1.40)
Intraventricular hemorrhage, grade 3 or 4, or death‡	179/653 (27.4)	156/661 (23.6)	1.18 (0.99–1.42)
Periventricular leukomalacia	24/631 (3.8)	30/641 (4.7)	0.83 (0.49–1.42)
Periventricular leukomalacia or death	149/654 (22.8)	132/662 (19.9)	1.18 (0.96–1.45)
Necrotizing enterocolitis, stage ≥2§	76/641 (11.9)	70/649 (10.8)	1.11 (0.82–1.51)
Necrotizing enterocolitis, stage ≥2, or death§	176/654 (26.9)	155/662 (23.4)	1.18 (0.98–1.43)
Pneumothorax	47/654 (7.2)	43/662 (6.5)	1.12 (0.74–1.68)
Postnatal corticosteroids for BPD	61/636 (9.6)	69/644 (10.7)	0.91 (0.67–1.24)
Death			
By 7 days	41/654 (6.3)	38/662 (5.7)	1.11 (0.72–1.72)
By 14 days	64/654 (9.8)	56/662 (8.5)	1.20 (0.84–1.70)
Late-onset sepsis	228/624 (36.5)	226/634 (35.6)	1.03 (0.89–1.18)
Late-onset sepsis or death	300/654 (45.9)	291/662 (44.0)	1.05 (0.94–1.18)
Patent ductus arteriosus	307/641 (47.9)	324/648 (50.0)	0.96 (0.86–1.07)
Treatment for patent ductus arteriosus			
Medical	219/634 (34.5)	233/645 (36.1)	0.95 (0.82–1.09)
Surgical	73/641 (11.4)	68/648 (10.5)	1.09 (0.80–1.48)
Any air leaks in first 14 days	51/654 (7.8)	42/662 (6.3)	1.23 (0.83–1.83)

* Values were adjusted for stratification factors (study center and gestational-age group) as well as for familial clustering. BPD denotes bronchopulmonary dysplasia.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% oxygen or the need for positive pressure support at 36 weeks or, in the case of infants requiring less than 30% oxygen, the need for any oxygen at 36 weeks after an attempt at oxygen withdrawal.

‡ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

§ There are three stages of necrotizing enterocolitis; higher stages indicate more severe necrotizing enterocolitis.

sults were observed for both gestational-age strata. Survival analysis with the use of the unadjusted Kaplan–Meier method (Fig. 2) and a Cox proportional-hazards model produced similar results (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; P=0.07). The rate of severe retinopathy among survivors who were discharged or transferred to another

facility or who reached the age of 1 year was lower in the lower oxygen-saturation group (8.6% vs. 17.9%; relative risk, 0.52; 95% CI, 0.37 to 0.73; P<0.001; number needed to treat, 11). Although use of bevacizumab was among the criteria for this outcome, only three infants received bevacizumab, and these infants also had threshold retin-

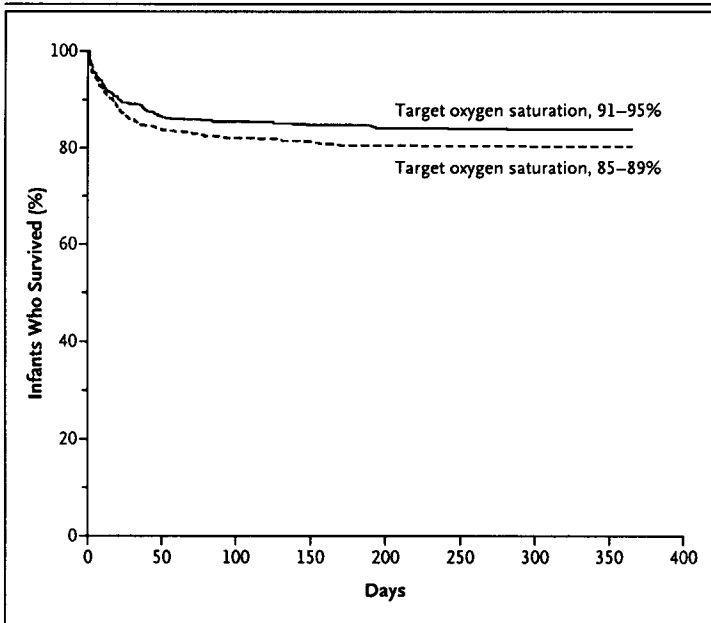


Figure 2. Kaplan-Meier Estimate of Survival to Hospital Discharge, Transfer, or 1 Year of Life.
 Cox proportional-hazards analysis indicated that there was an increased hazard of death in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group (hazard ratio, 1.28; 95% CI, 0.98 to 1.68; $P=0.07$). The analysis assumed that infants who were discharged or transferred from the hospital survived to 1 year of age.

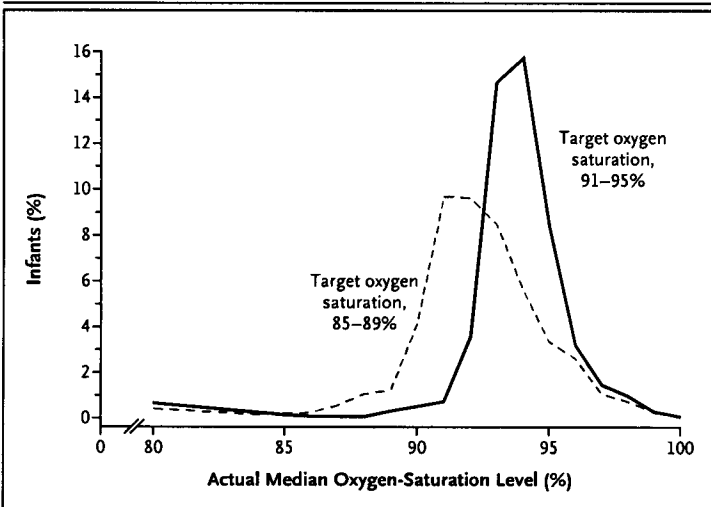


Figure 3. Actual Median Oxygen Saturation with Oxygen Supplementation in the Two Treatment Groups.
 The medians of the distributions were significantly different on the basis of a rank-sum test ($P<0.001$). The 80% oxygen-saturation level shown includes all values at or below 80%.

unchanged (Table 2 in the Supplementary Appendix).

SECONDARY OUTCOMES

The rate of oxygen use at 36 weeks was reduced in the lower-oxygen-saturation group as compared with the higher-oxygen-saturation group ($P=0.002$), but the rates of bronchopulmonary dysplasia among survivors, as determined by the physiological oxygen-saturation test at 36 weeks, and the composite outcome of bronchopulmonary dysplasia or death by 36 weeks did not differ significantly between the treatment groups. Other prespecified major outcomes also did not differ significantly between the two groups (Table 2).

The median oxygen-saturation level in infants who were receiving oxygen supplementation in the two treatment groups differed substantially but, as expected, there was considerable overlap (Fig. 3). The actual median levels of oxygen saturation were slightly higher than targeted levels in both treatment groups. The duration of oxygen supplementation was shorter in the lower-oxygen-saturation group, but the duration of mechanical ventilation, CPAP, and nasal synchronized intermittent mandatory ventilation did not differ significantly (Table 3 in the Supplementary Appendix). Other measures of resource use also did not differ significantly between the two groups.

DISCUSSION

In this multicenter, randomized trial, we found no significant difference in the primary outcome — severe retinopathy or death — between infants randomly assigned to a lower target range of oxygen saturation (85 to 89%) and those assigned to a higher target range (91 to 95%). Assessment of the individual components of the primary outcome showed that the lower target range of oxygen saturation increased the risk of in-hospital death, whereas it reduced the risk of severe retinopathy among survivors. These results were observed even though there was substantial overlap of actual oxygen-saturation levels between the two treatment groups. Previous trials of targeting of oxygen-saturation levels have shown similar difficulties in maintaining oxygen-saturation levels within a narrow target range.^{18,22} Longer follow-up will be required to determine the effects of lower target ranges of oxygen saturation on functional visual and neurodevelopmental outcomes.

opathy. Three ophthalmologists adjudicated results for the patients who did not meet the criteria for retinopathy, and the results were materially

Despite the increase in mortality when restrictive oxygen supplementation was used in the 1950s and 1960s and the limited data from observational studies,^{3-5,15,16} it is becoming common practice to use lower target ranges of oxygen saturation with the goal of reducing the risk of retinopathy of prematurity.²³ The results of this large randomized trial to test the effect of lower versus higher target ranges of oxygen saturation, in conjunction with the results of previous studies, add to the concern that oxygen restriction may increase the rate of death among preterm infants. The combined risk difference observed in the trials from the 1950s was an absolute increase in in-hospital mortality of 4.9 percentage points in the oxygen-restricted group,¹ which is close to the absolute increase of 3.7 percentage points in the rate of death before discharge in the lower-oxygen-saturation group that was observed in the current trial.

Randomized trials of oxygen restriction in preterm infants at least 2 weeks after birth¹⁸ or after moderately severe retinopathy developed²² did not show an increased risk of death or a significantly reduced risk of retinopathy in the lower-oxygen-saturation groups. However, the lower target ranges of oxygen saturation in these trials — 91 to 94% in one trial and 89 to 94% in the other — were closer to the target range in our higher-oxygen-saturation group. The increase in mortality in our trial may be related to the lower target ranges of oxygen-saturation levels, the use of oxygen restriction started soon after birth, or both. A meta-analysis of early restriction of oxygen supplementation based on trials from the 1950s to the 1970s showed a reduction in severe retinopathy (relative risk, 0.19; 95% CI, 0.07 to 0.50) with a nonsignificant trend toward increased mortality.²⁴ These trials were performed by limiting the FiO₂ concentration usually to less than

50%, at a time before the continuous monitoring of oxygen was possible. To our knowledge, no other randomized, controlled trials of different target ranges of oxygen saturation in supplementation initiated soon after birth have been performed since the availability of continuous transcutaneous oxygen-saturation monitoring. Like the meta-analysis²⁴ and most nonrandomized studies,^{3-5,15,16} our trial confirmed that lower target ranges of oxygenation result in a large reduction in the incidence of severe retinopathy among survivors. However, our data suggest that there is one additional death for approximately every two cases of severe retinopathy that are prevented. Several ongoing trials across the world address the same intervention tested in the current trial.²⁵

In summary, a target range of oxygen saturation of 85 to 89%, as compared with a range of 91 to 95%, did not affect the combined outcome of severe retinopathy or death, but it increased mortality while substantially decreasing severe retinopathy among survivors. At the present time, caution should be exercised regarding a strategy of targeting oxygen-saturation levels in the low range for preterm infants, since it may lead to increased mortality.

Supported by Supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, and U10 HD53124); the National Heart, Lung, and Blood Institute; and the National Institutes of Health (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, U11 RR25008, U11 RR24139, U11 RR24979, and U11 RR25744). Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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ORIGINAL ARTICLE

Early CPAP versus Surfactant in Extremely Preterm Infants

The NICHD Neonatal Research Network and the SUPPORT Study Group*

ABSTRACT

BACKGROUND

There are limited data to inform the choice between early treatment with continuous positive airway pressure (CPAP) and early surfactant treatment as the initial support for extremely-low-birth-weight infants.

METHODS

We performed a randomized, multicenter trial, with a 2-by-2 factorial design, involving infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation. Infants were randomly assigned to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen).

RESULTS

A total of 1316 infants were enrolled in the study. The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% confidence interval [CI], 0.85 to 1.05) after adjustment for gestational age, center, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia ($P<0.001$), required fewer days of mechanical ventilation ($P=0.03$), and were more likely to be alive and free from the need for mechanical ventilation by day 7 ($P=0.01$). The rates of other adverse neonatal outcomes did not differ significantly between the two groups.

CONCLUSIONS

The results of this study support consideration of CPAP as an alternative to intubation and surfactant in preterm infants. (ClinicalTrials.gov number, NCT00233324.)

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This article (10.1056/NEJMoa0911783) was published on May 16, 2010, at NEJM.org.

N Engl J Med 2010.
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IT HAS BEEN SHOWN THAT SURFACTANT treatment at less than 2 hours of life significantly decreases the rates of death, air leak, and death or bronchopulmonary dysplasia in preterm infants.^{1,2} Overall, prophylactic treatment with surfactant has not been shown to significantly reduce the risk of bronchopulmonary dysplasia alone, whereas studies comparing early with later rescue use of surfactant have shown that there is a decreased risk of chronic lung disease with early use.² Several studies have shown that the use of surfactant does not have a significant effect on the risk of subsequent neurodevelopmental impairment,³ although a recent follow-up assessment of infants involved in a randomized trial showed that early surfactant treatment (at a mean of 31 minutes of age) as compared with later surfactant treatment (at a mean of 202 minutes of age) was associated with a significantly higher rate of increased muscle tone in the infants and a delay in the infants' ability to roll from the supine to the prone position.⁴ However, in many of the trials of surfactant treatment, the rate of maternal corticosteroid therapy before delivery — an intervention known to improve neonatal survival⁵ and decrease the rate of complications — was not high, and none of the infants in the control group received early treatment with continuous positive airway pressure (CPAP). There is a growing body of observational evidence suggesting that in the case of very preterm infants with respiratory distress who are not treated initially with surfactant, the early use of CPAP may decrease the need for mechanical ventilation without an increase in complications.⁶⁻¹¹

In a study reported in a recent issue of the *Journal*, 610 infants, born between 25 weeks 0 days and 28 weeks 6 days of gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress at that time, were randomly assigned to either intubation and ventilation or CPAP at a pressure of 8 cm of water; infants who were randomly assigned to CPAP were intubated if they met certain criteria for the failure of CPAP treatment.¹² There was no significant reduction in the CPAP group, as compared with the intubated group, in the rate of death or the need for supplemental oxygen at 36 weeks (the primary outcome), and there was a significantly higher rate of pneumothorax in the CPAP group than in

the intubated group (9.1% vs. 3.0%); most of the cases of pneumothorax occurred within the first 2 days, which is consistent with the findings of a previous meta-analysis.¹³

We designed the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT) to compare early CPAP treatment with early surfactant treatment in extremely preterm infants. Using a factorial design, we also randomly assigned infants to one of two target ranges of oxygen saturation during their exposure to supplemental oxygen.

METHODS

STUDY DESIGN

In this randomized, multicenter trial, we compared a strategy of treatment with CPAP and protocol-driven limited ventilation begun in the delivery room and continued in the neonatal intensive care unit (NICU) with a strategy of early intratracheal administration of surfactant (within 1 hour after birth) followed by a conventional ventilation strategy. In a 2-by-2 factorial design, infants were also randomly assigned to one of two target ranges of oxygen saturation (85 to 89% or 91 to 95%) until the infant was 36 weeks of age or no longer received ventilatory support or supplemental oxygen. The results of this portion of the study are discussed elsewhere in this issue of the *Journal*.¹⁴ Randomization was stratified according to center and gestational-age group, with the use of specially prepared double-sealed envelopes, and was performed before the actual delivery. Infants who were part of multiple births were randomly assigned to the same group. Written informed consent from a parent or guardian for an infant's participation in the trial was required before delivery.

Infants were eligible for inclusion in the study if they were 24 weeks 0 days to 27 weeks 6 days of gestation at birth according to the best obstetrical estimate, if they were born without known malformations at a participating center, if a decision had been made to provide full resuscitation for them, and if written informed consent had been obtained from a parent or guardian. The infants were randomly assigned within each center and within each gestational-age stratum (24 weeks 0 days to 25 weeks 6 days or 26 weeks 0 days to 27 weeks 6 days).

The study was conducted as part of the Neonatal Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The study was approved by the human subjects committee at each participating site and at RTI International, which is the data center for the Neonatal Research Network. Data collected at participating sites were transmitted to RTI International, which stored, managed, and analyzed the data for this study.

CPAP GROUP

In the delivery room, CPAP was administered by means of a T-piece resuscitator, a neonatal ventilator, or an equivalent device. CPAP or ventilation with positive end-expiratory pressure (PEEP) (at a recommended pressure of 5 cm of water) was used if the infant received positive-pressure ventilation during resuscitation. CPAP was continued until the infant's admission to the NICU. Intubation was not performed for the sole purpose of surfactant administration in infants who were randomly assigned to the CPAP group, but infants who required intubation for resuscitation on the basis of standard indications specified in the Neonatal Resuscitation Program guidelines¹⁵ were given surfactant within 60 minutes after birth.

In the NICU, infants who were randomly assigned to CPAP could be intubated if they met any of the following criteria: a fraction of inspired oxygen (FiO_2) greater than 0.50 required to maintain an indicated saturation of peripheral oxygen (SpO_2) at or above 88% for 1 hour; a partial pressure of arterial carbon dioxide ($PaCO_2$) greater than 65 mm Hg, documented by a single measurement of blood gases within 1 hour before intubation; or hemodynamic instability, defined as a blood pressure that was low for gestational age, poor perfusion, or both, requiring volume or pressor support for a period of 4 hours or more. Infants who were intubated within the first 48 hours after birth were to receive surfactant. After an infant's admission to the NICU, the unit used its standard method for the delivery of CPAP — that is, a ventilator, a purpose-built flow driver, or a bubble CPAP circuit.

Extubation of an infant in the CPAP group was to be attempted within 24 hours after the infant met all of the following criteria: a $PaCO_2$ below 65 mm Hg with a pH higher than 7.20, an SpO_2 above 88% with an FiO_2 below 0.50, a mean air-

way pressure of less than 10 cm of water, a ventilator rate of less than 20 beats per minute, an amplitude of less than twice the mean airway pressure if high-frequency ventilation was being used, hemodynamic stability, and the absence of clinically significant patent ductus arteriosus. Criteria for reintubation were the same as those for initial intubation. After three intubations, infants in the CPAP group received treatment according to the standard practice in the NICU to which they had been admitted.

SURFACTANT GROUP

All the infants in the surfactant group were to be intubated in the delivery room and were to receive surfactant within 1 hour after birth with continued ventilation thereafter. The infants were to be extubated within 24 hours after meeting all of the following criteria: a $PaCO_2$ of less than 50 mm Hg and a pH higher than 7.30, an FiO_2 of 0.35 or less with an SpO_2 of 88% or higher, a mean arterial pressure of 8 cm of water or less, a ventilator rate of 20 beats per minute or less, an amplitude of less than twice the mean arterial pressure if high-frequency ventilation was being used, and hemodynamic stability without evidence of clinically significant patent ductus arteriosus. Once the infants were extubated, they were treated according to the standard practice in the NICU to which they had been admitted.

The criteria for both groups were in effect for the infants' first 14 days of life, after which the infants were treated according to the standard practice in the NICU to which they had been admitted. In the case of both groups, intubation could be performed at any time if there was an episode of repetitive apnea requiring bag-and-mask ventilation, clinical shock, or sepsis, or if surgery was required.

OUTCOMES

The primary outcome was death or bronchopulmonary dysplasia. Bronchopulmonary dysplasia was defined according to the physiological definition, as the receipt of more than 30% supplemental oxygen at 36 weeks or the need for positive-pressure support or, in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen.^{16,17} Prespecified secondary outcomes included bronchopulmonary dys-

plasia as defined by the receipt of any supplemental oxygen at 36 weeks. Prespecified safety outcomes included death, pneumothorax, intraventricular hemorrhage, and the need for chest compressions or epinephrine during resuscitation.

STATISTICAL ANALYSIS

The sample-size calculations were based on data from the Neonatal Research Network from the year 2000, which showed that the rate of death or survival with bronchopulmonary dysplasia at 36 weeks was 67% and the rate of death or survival with neurodevelopmental impairment at 18 to 22 months was 61%. We hypothesized that with early CPAP there would be a reduction of 10% in the incidence of these complications. We increased the sample size by a factor of 1.12 to allow for infants in multiple births to be randomly assigned to the same treatment, because this introduced a clustering effect into the design, and we increased the sample sizes by an additional 17% to adjust for loss to follow-up after discharge. We increased the sample size further to minimize type I error with the use of a conservative 2% level of significance. The result was a target sample of 1310 infants. We planned to test for an interaction between the two factorial parts of the study, but the study was not powered for that analysis.

Analyses were performed according to the intention-to-treat principle. The denominator that was used to calculate the rate of each outcome was the number of infants for whom that outcome was known. The primary analyses focused on the percentage of infants in each group who survived to 36 weeks of postmenstrual age without bronchopulmonary dysplasia. Analysis of this and all other categorical outcomes was performed with the use of robust Poisson regression in a generalized-estimating-equation model to obtain adjusted relative risks with 95% confidence intervals. Continuous outcomes were analyzed with the use of mixed-effects linear models to obtain adjusted means and standard errors.

In the analysis of all outcomes, the results were adjusted, as prespecified, for gestational-age strata, center, and familial clustering. Two-sided P values of less than 0.05 were considered to indicate statistical significance, and no adjustments have been made for multiple comparisons. An independent data and safety monitoring committee reviewed the interim safety and efficacy results —

Figure 1 (facing page). Screening, Randomization, and Primary Outcome.

The numbers in the figure exclude pregnant women who were screened but whose babies were not subsequently born at a study center between 24 weeks 0 days and 27 weeks 6 days of gestation. Postmenstrual age is defined as the gestational age plus the postnatal age. BPD denotes bronchopulmonary dysplasia according to the physiological definition (receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of oxygen).^{16,17}

including those related to adverse outcomes — four times. Lan-DeMets spending functions with Pocock and O'Brien-Fleming boundaries were used to determine stopping rules for interim safety and efficacy monitoring, respectively.

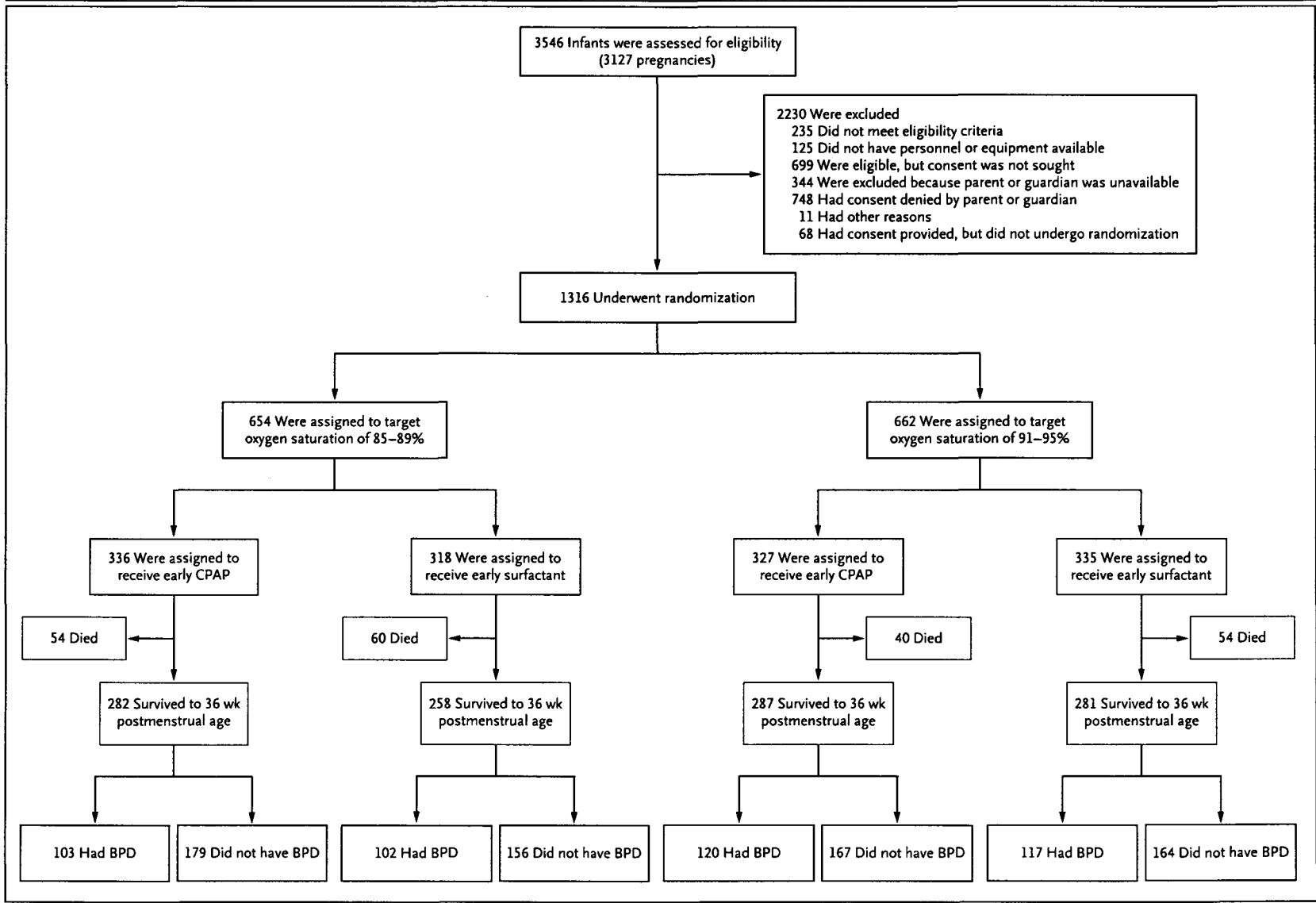
For the 46 planned analyses of secondary outcomes according to treatment, we would expect no more than 3 tests to have P values of less than 0.05 on the basis of chance alone. Subgroup analyses were conducted within prespecified gestational-age strata for 36 predefined outcomes. Although these tests have not been adjusted for multiple comparisons, we would expect no more than 2 tests per stratum to have P values of less than 0.05 on the basis of chance alone.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

From February 2005 through February 2009, a total of 1316 infants were enrolled, of whom 565 were in the lower gestational-age stratum (24 weeks 0 days to 25 weeks 6 days) and 751 were in the higher stratum (26 weeks 0 days to 27 weeks 6 days) (Fig. 1). There were no significant differences between the two treatment groups with respect to sex, birth weight, or race or ethnic group (Table 1).

Delivery room interventions in the two groups are summarized in Table 2. The rates of intubation in the delivery room and of the use of positive-pressure ventilation or epinephrine to treat persistent bradycardia were significantly lower among infants randomly assigned to CPAP than among those assigned to surfactant treatment. Overall, 32.9% of the infants in the CPAP group did not receive surfactant during their hospitalization.



Variable	CPAP (N = 663)	Surfactant (N = 653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus-minus values are means ±SD. None of the comparisons were significant. CPAP denotes continuous positive airway pressure.

† Race or ethnic group was reported by the mother or guardian of each child.

PRIMARY OUTCOME

After adjustment for gestational age, center, and familial clustering, the rates of the primary outcome of death or bronchopulmonary dysplasia as assessed according to the physiological definition did not differ significantly between the two groups. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks. When components of this composite outcome were analyzed separately, there was no significant between-group difference in the rate of death or the rate of bronchopulmonary dysplasia (Table 3).

There was no significant interaction between the two interventions assessed in the trial with respect to the primary outcome of death or bronchopulmonary dysplasia as assessed either according to the physiological definition ($P=0.59$) or according to the need for any supplemental oxygen at 36 weeks ($P=0.53$). There was no signifi-

cant interaction between gestational-age stratum and treatment strategy with respect to the primary outcome ($P=0.84$ with the physiological definition of bronchopulmonary dysplasia and $P=0.44$ with bronchopulmonary dysplasia defined according to the need for any supplemental oxygen at 36 weeks), and there was no significant between-group difference in the rate of the primary outcome (with either definition of bronchopulmonary dysplasia) in either gestational-age stratum.

SECONDARY OUTCOMES

More infants in the CPAP group than in the surfactant group were alive and free from the need for mechanical ventilation by day 7 ($P=0.01$), and infants in the CPAP group required fewer days of ventilation than did those in the surfactant group ($P=0.03$). There were no significant between-group differences in the rates of air leak in the first 14 days, pneumothorax during the hospital stay, necrotizing enterocolitis requiring medical or surgical treatment, patent ductus arteriosus requiring surgery, severe intraventricular hemorrhage, or severe retinopathy of prematurity, as defined according to the new type 1 threshold in the Early Treatment for Retinopathy of Prematurity study (ETROP; ClinicalTrials.gov number, NCT00027222)¹⁸ or according to the need for surgical intervention among survivors. One infant in the surfactant group died in the delivery room at 21 minutes after birth and was not intubated; 83.1% of the infants in the CPAP group were intubated ($P<0.001$). The rate of use of postnatal corticosteroids to treat bronchopulmonary dysplasia was lower in the CPAP group than in the surfactant group ($P<0.001$) (Table 3). The other secondary outcomes are shown in Table 3.

In post hoc stratified analyses of secondary outcomes, among infants who were born between 24 weeks 0 days and 25 weeks 6 days of gestation, the rates of death during hospitalization and at 36 weeks were significantly lower in the CPAP group than in the surfactant group (rate of death during hospitalization: 23.9% vs. 32.1%; relative risk with CPAP, 0.74; 95% confidence interval [CI], 0.57 to 0.98; $P=0.03$; rate of death at 36 weeks: 20.0% vs. 29.3%; relative risk, 0.68; 95% CI, 0.5 to 0.92; $P=0.01$ [see Table A1 in the Supplementary Appendix]); in contrast, there was no significant between-group difference in the rate of death during hospitalization or at 36 weeks among the in-

Table 2. Apgar Scores of Newborns and Interventions in the Delivery Room and NICU.*

Variable	CPAP (N = 663) no./total no. (%)	Surfactant (N = 653) no./total no. (%)	Relative Risk with CPAP (95% CI)	Adjusted P Value
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CPAP denotes continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

fants who were born between 26 weeks 0 days and 27 weeks 6 days of gestation (rate of death during hospitalization: 10.8% and 10.2%, respectively) rate death of 36 weeks: 9.8% and 8.6%, respectively (see Tables A1 and A3 in the Supplementary Appendix, available with the full text of this article at NEJM.org).

DISCUSSION

In this multicenter, randomized trial involving extremely preterm infants, there was no significant difference between a strategy of early CPAP and limited ventilation and a strategy of early intubation and surfactant administration within 1 hour after birth with respect to the rate of the composite primary outcome of death or bronchopulmonary dysplasia. We used the physiological definition of bronchopulmonary dysplasia, since it includes as a specification an attempt to withdraw supplemental oxygen from infants receiving less than 30% oxygen at 36 weeks, in order to confirm their need for supplemental oxygen.^{16,17} Plausible results, on the basis of the 95% confidence intervals for the relative-risk estimates, included a risk of death or bronchopulmonary dysplasia in the CPAP group that was between 85

and 105% of that in the surfactant group. The results were similar in secondary analyses in which bronchopulmonary dysplasia was defined according to the use of any supplemental oxygen at 36 weeks.

We did not include infants who were born at a gestational age of less than 24 weeks, since the results of a pilot trial showed that 100% of such infants required intubation in the delivery room.¹⁹ A retrospective study showed that some infants in this gestational-age group can be treated successfully with early CPAP, but the majority require intubation.²⁰

There was a high rate of intubation and surfactant treatment among infants assigned to CPAP, but this was anticipated, given the design of the study, which was to test an initial strategy of early CPAP as compared with early intubation and surfactant, with crossover planned for ethical reasons in the case of infants in whom CPAP treatment was not successful. Our trial differs from the trial of Morley et al.¹² in that we randomly assigned all eligible preterm infants to a treatment group, irrespective of whether they were breathing spontaneously or whether they had respiratory distress that warranted intervention, and in that we included infants who were born as early

Table 3. Selected Prespecified Outcomes.*

Outcome	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.^{16,17}

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.

as 24 weeks of gestation. In the study by Morley et al., surfactant was not administered routinely in the intubation group. Our protocol, which called for early CPAP and a determination of the need for intubation, was based on the findings of previous observational studies showing that Neonatal Research Network sites that had the most experience with CPAP also used a higher threshold for intubation and the initiation of mechanical ventilation than did sites with less experience.⁴⁻⁶ The infants who were randomly assigned to surfactant treatment in our trial were

treated with a ventilation approach that was used by a majority of the Neonatal Research Network sites before the trial began. We believed that comparing these two methods would provide more clinically relevant results. Data are currently being collected to assess survival without neurodevelopmental impairment at 18 to 22 months.

We found no significant between-group differences in the rates of pneumothorax, intraventricular hemorrhage, or the need for chest compressions or epinephrine in the delivery room, and the rates were similar to those among infants in the Neonatal Research Network population who were born between 2000 and 2004 at similar gestational ages. The rate of air leaks in the first 14 days of life was not increased with the use of early CPAP at a pressure of 5 cm of water, as compared with the use of early surfactant.

In secondary analyses stratified according to gestational age at birth, there was a significant reduction in the risk of death in the CPAP group, as compared with the early-intubation group, among infants born between 24 weeks 0 days and 25 weeks 6 days of gestation but not among infants who were born at a later gestational age. Given the fact that there was no significant interaction between the intervention and gestational age, the post hoc nature of these analyses, and the number of secondary analyses performed, this observation must be interpreted with caution, and

further testing should be performed in this immature population.

In summary, we found no significant difference in the primary outcome of death or bronchopulmonary dysplasia between infants randomly assigned to early CPAP and those assigned to early surfactant treatment. In secondary analyses, the CPAP strategy, as compared with early surfactant treatment, resulted in a lower rate of intubation (both in the delivery room and in the NICU), a reduced rate of postnatal corticosteroid use, and a shorter duration of ventilation without an increased risk of any adverse neonatal outcome. These data support consideration of CPAP as an alternative to routine intubation and surfactant administration in preterm infants.

Supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124), cofunding from the National Heart, Lung, and Blood Institute, and grants from the National Institutes of Health (M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744).

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank our medical and nursing colleagues and the infants and their parents who agreed to take part in this study.

APPENDIX

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Eunice Kennedy Shriver
National Institute of Child Health
and Human Development (NICHD)
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Embargoed For Release

Sunday, May 16, 2010

1 p.m. EDT

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Higher Oxygen Levels Improve Preterm Survival, Increase Risk for Eye Condition
Early CPAP as Effective For Premies as Ventilator, With Fewer Complications

Two findings from an NIH research network study provide new information on how much oxygen very preterm infants should receive starting on the first day of life and the most effective means to deliver it to them.

The first was that higher oxygen levels improve preterm infants' survival but increase the risk for a condition that can damage the retina.

The second was that a treatment typically used for adults with sleep apnea also is as effective as the traditional ventilator and surfactant therapy used to treat breathing difficulties in preterm infants—and may result in fewer complications. The treatment relies on a continuous positive airway pressure (CPAP) machine to blow air through a preterm infant's nostrils, to gently inflate the lungs.

These findings appear in two articles published online by The New England Journal of Medicine. The study results also will be presented on May 16 at the American Thoracic Society 2010 International Conference in New Orleans.

“Until the current study, CPAP had shown promise in treating respiratory distress in preterm infants, but had never been compared to ventilator therapy in this group of patients,” said Alan E. Guttmacher, M.D., acting director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), one of the NIH

Institutes that provided infrastructure and funding for the study. “The study results indicate that CPAP is an effective initial alternative to ventilator therapy for very preterm infants of 24-27 weeks gestational age.”

The study was conducted by the 20 academic medical centers participating in the NICHD’s Neonatal Research Network. The study also received funding from the NIH’s National Heart, Lung, and Blood Institute.

The lead author of the article comparing oxygen saturation levels was Waldemar A. Carlo, M.D., of the University of Alabama at Birmingham. The lead author of the article comparing CPAP therapy to ventilator and surfactant therapy was Neil N. Finer, M.D., of the University of California at San Diego. The NICHD author of both papers was Rosemary D. Higgins, M.D.

“Balancing the benefits of supplemental oxygen against the risks in these very premature babies has been a concern of doctors and parents for decades,” said NHLBI Acting Director Susan B. Shurin, M.D., a board-certified pediatrician. “The results of this large clinical trial of extremely low birthweight infants will help inform management decisions to improve chances of survival and reduce complications associated with breathing problems in these vulnerable patients.”

The study enrolled 1,316 babies born between the 24th and 27th weeks of pregnancy. A full-term pregnancy is 40 weeks long. The very premature babies in the study had an average weight of less than two pounds.

The study was divided into two arms that provided the findings for the articles. Each arm proceeded at the same time, in the same group of infants. In the first arm, each infant had a 50 percent chance of receiving higher oxygen target saturation levels, and a 50 percent chance of receiving lower levels. In the second arm, each infant had a 50 percent chance of receiving oxygen by CPAP and a 50 percent chance of receiving intubation with surfactant, a viscous substance that helps keep the lungs’ air sacs open. Although surfactant normally is produced by the lung, premature infants are not ready to make surfactant at first and suffer from severe breathing difficulties.

Researchers Compare Higher Oxygen Levels To Lower Levels

Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP. [Information on ROP](http://www.nei.nih.gov/health/rop/rop.asp) (<http://www.nei.nih.gov/health/rop/rop.asp>) is available from the National Eye Institute.

For the arm of the study that compared oxygen levels, the infants were assigned at random to receive oxygen at one of two levels. The lower level consisted of 85 to 89 percent oxygen saturation in the babies’ blood; the higher level 91 to 95 percent. The

infants also were assigned at random to receive oxygen either through a ventilator or a CPAP machine.

The researchers evaluated the infants at the two oxygen saturation levels in a single combined measure, referred to as the combined outcome of their survival and their likelihood of experiencing ROP. No overall difference emerged between the groups in terms of this measure. However, there was a striking difference when survival and likelihood of experiencing ROP were considered separately.

More of the infants on the low oxygen level died than did infants on the higher level: 19.9 percent compared to 16.2 percent. But among those who survived, fewer on the lower level of oxygen developed ROP: 8.6 percent versus 17.9 percent in the higher-oxygen group.

“Many doctors believe that optimal oxygen saturation levels fall between 85 and 95 percent,” Dr. Carlo said. “Our results offer much needed data on which to base treatment decisions.”

CPAP Compared to Traditional Ventilator-Surfactant Therapy

A second arm of the study compared the standard ventilator treatment and surfactant for preterm respiratory distress to treatment with CPAP (http://www.nhlbi.nih.gov/health/dci/Diseases/cpap/cpap_what.html), which involves passing air through an infant’s nose via prongs that rest in the nostrils. The standard ventilator (http://www.nhlbi.nih.gov/health/dci/Diseases/vent/vent_what.html) treatment involves placing a breathing tube in a newborn’s windpipe to provide oxygen and surfactant. It is not possible to deliver surfactant with CPAP.

In this arm of the study, newborns who were randomly assigned to the ventilator-surfactant treatment had a breathing tube placed in their windpipes within an hour of birth and received a dose of surfactant. Those who obtained CPAP treatment received oxygen through prongs placed in their nostrils, also within the first hour of life. Any infant receiving CPAP who subsequently did not achieve adequate oxygen levels in their blood was placed on a ventilator. Of the infants who received CPAP treatment initially, 83 percent required a ventilator tube in the windpipe and 67 percent received surfactant.

“Surfactant and intubation together have been shown to reduce the risk of serious complications and death in preterm infants,” Dr. Finer said. “But the use of CPAP also grew during the last 10 or 15 years, without randomized studies to test it and compare it to surfactant.”

The researchers looked at mortality and at a lung condition called bronchopulmonary dysplasia, which is characterized by a need for oxygen therapy when the baby is four weeks short of his or her original due date, or 36 weeks after the mother’s last menstrual period. When researchers compared CPAP to surfactant on a combined measure of

mortality and bronchopulmonary dysplasia, the two types of breathing therapy were practically identical.

“The study shows that CPAP is an effective alternative to surfactant in preterm infants,” Dr. Higgins said. “Because it is less invasive than ventilator therapy, CPAP appears to be an appropriate first treatment for preterm newborns. If CPAP is unsuccessful, an infant can be placed on a ventilator and given surfactant.”

By other measures, children initially placed on CPAP actually fared somewhat better than children who had received surfactant with the ventilator. They were more likely to have survived and to not require breathing therapy a week after being born. They were also less likely to need steroid treatment for their lungs; and they spent less time overall on ventilators.

Furthermore, the earliest preterm infants in the study, born at 24 to 25 weeks gestation, were less likely to die if they had received CPAP than if they had received surfactant as the initial treatment in the study.

The team will evaluate the children again when they are 18 to 22 months old, to learn whether any differences arise among the children who took part in the different treatments arms of the study.

For more information on this study (NCT 00233324), visit www.clinicaltrials.gov.

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The NICHD sponsors research on development, before and after birth; maternal, child, and family health; reproductive biology and population issues; and medical rehabilitation. For more information, visit the Institute’s Web site at <http://www.nichd.nih.gov/>.

Part of the National Institutes of Health, the National Heart, Lung, and Blood Institute (NHLBI) plans, conducts, and supports research related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders. The Institute also administers national health education campaigns on women and heart disease, healthy weight for children, and other topics. NHLBI press releases and other materials are available online at <http://www.nhlbi.nih.gov>.

The National Institutes of Health (NIH) —The Nation’s Medical Research Agency— includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical, and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit <http://www.nih.gov>.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: McGrath, John (NIH/NICHD) [E]
Subject: FW: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS*****
Date: Tuesday, May 11, 2010 1:07:00 PM
Importance: High

John

This is the type of email I have sent previously about these two papers.

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, April 21, 2010 10:46 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Nancy Newman; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); (susie.buchter@oz.ped.emory.edu); 'Brenda Morris'; Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; vineet.bhandari@yale.edu; 'Sood, Beena'; 'Michael O`Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; Cunningham, Meg; 'Huitema, Carolyn Petrie'
Subject: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS*****
Importance: High

Hi,

We have been informed by NEJM that both SUPPORT Papers will be *accelerated Online First release* scheduled to coincide with the presentations of the results at the American Thoracic Society's annual meeting on Sunday May 16, 2010. The on-line release will occur at 1 PM EDT on 5/16/2010. The print publication is slated to appear in the May 27, 2010 issue of NEJM.

As far as I know, this will be a first for the Neonatal Research Network.

The SUPPORT abstracts will be presented in platforms at PAS. Neil will deliver the same talks will be given at a post-PAS meeting on neonatal resuscitation.

We are not to discuss the fact that the papers have been reviewed or accepted by NEJM. PI's - please insure that all of your staff with the confidential knowledge regarding the SUPPORT papers are aware of the NEJM rules!! This is particularly important for those attending the PAS meeting who may be asked about the status of the papers. **If asked, the appropriate response is "The**

manuscripts are in the peer review process.”

In addition, since the papers are not yet published in NEJM, we need to respect their embargo policy. This means that we are requested to follow the guidelines at <http://authors.nejm.org/Help/Embargo.asp>.

Specifically, the guidelines state:

- Please do not discuss the fact that the research has been submitted or accepted for publication in the *New England Journal of Medicine*.
- Please do not distribute any copies of the manuscript, tables, or figures. (It is acceptable to use the materials in a presentation, but they should not be distributed.)

THANKS TO ALL OF YOU AND YOUR STAFF FOR THE EFFORT INVOLVED IN THIS LANDMARK STUDY.

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

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From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Final remarks for Preterm oxygen briefing
Date: Wednesday, May 12, 2010 1:27:33 PM

OK. I guess the call is over.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, May 12, 2010 1:20 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Final remarks for Preterm oxygen briefing

This is fine - did it sound ok?

-----Original Message-----

From: Bock, Robert (NIH/NICHD) [E]
Sent: Wednesday, May 12, 2010 1:20 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Final remarks for Preterm oxygen briefing

Sorry I missed this.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, May 06, 2010 10:04 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: Re: Final remarks for Preterm oxygen briefing

Bob

One clarification - the NRN currently has 16 sites. There were 20 sites total in the current study as it overlapped two cycles: 4 sites fell out and 4 were added de to the re-competition that occurred in 2006. Can i say "mutiple" site instead of 20 sites? We have never had 20 total sites. This is minor but - want to insure accuracy

Thanks
Rose

From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: McGrath, John (NIH/NICHD) [E]; Miller, Marianne Glass (NIH/NICHD) [E]
Sent: Thu May 06 18:32:18 2010
Subject: Final remarks for Preterm oxygen briefing

Hi all. Attached is the final copy of Rose's remarks for the preterm oxygen studies briefing on the 12th. John and Marianne, these are also in the "Preterm Oxygen Studies" folder in the 2010 releases folder on the N: Drive.

Thanks.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Webb, Robin E."
Subject: RE: SUPPORT data queries
Date: Monday, May 10, 2010 10:58:00 AM

After the SC meeting

Thanks
Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Wednesday, May 05, 2010 2:10 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT data queries

Hi Rose,

For this and the protocol, do you want to poll for before the SC meeting? Or start the following week?

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, May 05, 2010 12:14 PM
To: Webb, Robin E.
Cc: Archer, Stephanie (NIH/NICHD) [E]; Das, Abhik; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT data queries

Robin
Can you send to the SUPPORT subcommittee and set up a call??

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Michael Cotten [mailto:cotte010@mc.duke.edu]
Sent: Saturday, May 01, 2010 8:19 PM
To: Neil Finer; Wally Carlo, M.D.
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Ronald N Goldberg
Subject: SUPPORT data queries

Hi Neil and Wally, Rose and Ron...

first..congratulations on the first presentation of results and publication of the manuscripts!!!!

here are two secondary data analysis proposals for SUPPORT,,,one looking at the DR CPAP portion of the study, the other at the oxygen sat target portion.

thanks

mc

C. Michael Cotten MD MHS
Associate Professor of Pediatrics
Medical Director Neonatology Clinical Research
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2424 Erwin Road Suite 504
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From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: support breathing outcomes
Date: Monday, May 10, 2010 10:51:46 AM
Attachments: [Form_SUPF03, SUPPORT Pulmonary Outcomes, 2006-04-10.pdf](#)
[Form_SUPF00, SUPPORT Pulmonary Outcomes, 2005-12-12.pdf](#)
[Form_SUPF01, SUPPORT Pulmonary Outcomes, 2005-12-12.pdf](#)
[Form_SUPF02, SUPPORT Pulmonary Outcomes, 2006-04-17.pdf](#)

Dear Rose,

Hope you enjoyed PAS and had a little time to explore Vancouver (you had a busy schedule ☺). Our prematurity and respiratory outcomes program (PROP) was just awarded (start 5/1). Alan Jobe is one of the PIs, and would like to make use of the breathing outcomes surveys that were developed for PROP. We are having a meeting of the pulmonology co-Is and PIs (neonatologists) at ATS and I would like to distribute some of the SUPPORT breathing outcome CRFs as a starting point for discussions on developing tools to assess respiratory disease risk/phenotyping in NICU grads.

Attached are the ones Alan and I were thinking of distributing, but wanted your input on what can and cannot be shared. The MOP is something that looks like I should NOT distribute.

How was the feedback at PAS about SUPPORT?

Thanks, Carol

Carol J. Blaisdell, M.D.
Medical Officer
Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

Administered At 18-22 Months Corrected Age

This interview should be administered by a trained study interviewer. The target window for this interview is between 18-22 months' corrected age.

_____ (Child's name)

All questions pertain only to his/her health.

Introduction Script:

When parent or primary care giver is on phone:

Hello, my name is <your name>. I am calling from the <NICHD Center>. As you probably remember, when you were in the NICU you enrolled in our study about respiratory health of premature infants. I am calling to ask you some questions about your baby's breathing. It will take about 10-20 minutes to complete. Is this a good time for you?

As with all information we collect, the answers to these questions will be kept confidential.

Before we begin this interview, it would be helpful if you could gather any notes you have about your baby's breathing as well as any medications your child has been prescribed or has been taking and have them in front of you.

Interview Outcome

Was the interview conducted? 1• Yes 2• No

If No why? 1• Loss of contact 2• Interviewee refused 3• Child died 4• Other SPECIFY _____

Initials of person completing this form. _____

1. TODAY'S DATE: |_|_| - |_|_| - |_|_|_|_|_|
 mm dd yyyy

PLEASE CONFIRM PERSONAL INFORMATION AND MAKE NECESSARY CORRECTIONS.

Child's Name: _____
 (first) (last)

Child's Birthdate: |_|_| - |_|_| - |_|_|_|_|_|
 mm dd yyyy

Telephone Number _____ - _____ - _____

Address _____

Which relative is most likely to have your address in case we lose contact with you?

Name	Relationship
Address	
Telephone	
Cell Phone	
Email	

Enter name and relationship code of the person being interviewed*:

2a. Name: _____ 2b. Relationship Code: |_|_|_|

- 001 - Mother of Child
 - 002 - Father of Child
 - 301 - Adoptive mother
 - 302 - Adoptive father

 - Other: _____
- Common codes are listed here for other relationships, please look up relationship code from Appendix D of the Breathing Outcomes Manual of Operations and enter above.*

3. Type of Interview: 1[•] Face to Face 2[•] Telephone

4. Location of Interviewer: 1[•] Local Center 2[•] Rochester
 (Option 1) (Option 2)

Instructions:

Parents or guardians expressing concerns regarding their child's breathing should be advised to discuss them with the family's primary care physician.

Where the phrase "last contact" is used below, please substitute with the most specific relevant time prompt, e.g. for the 18-22 month interview, refer to "over the past 6 months", etc.

Interview begins:

Some of these questions will be familiar to you. Since we last spoke (___) months ago on (___/___/___) we want to learn what changes, if any, there have been to your child's health. We are especially interested in any breathing problems your child may have.

5. Has the child been with you over the past 6 months? 1[•] Yes 2[•] No

Since our last contact with you about your child...

6. How many times has your child visited a doctor's office? |_|_| times

6a. How many of these times were because of wheezing or breathing problems? |_|_| times

Since our last contact with you about your child...

7. How many times has your child visited an Emergency Department (Emergency room)? |_|_| times

7a. How many of these times were because of wheezing or breathing problems? |_|_| times

Since our last contact with you about your child...

8. How many times has your child stayed in the hospital one or more nights in a row? |_|_| times

8a. How many of these times were because of wheezing or breathing problems? |_|_| times

The next questions are about your baby's breathing.

The first question is about wheezing. By wheezing we mean an expiratory sound (a sound that is made when breathing out, not in) that comes from the chest, sometimes described as whistling or musical.

9. Since our last contact with you, has your baby's chest sounded wheezy or whistling?

- 1• Yes 2• No 3• Don't Know *Ask Question 9a for all responses*

9a. "Has your baby's breathing sounded like this?" (*play audio clip of wheezing*).

- 1• Yes 2• No 3• Don't Know

IF YES TO QUESTION 9 or 9a:

9b. Has this occurred with colds?

- 1• Yes
2• No
3• Sometimes

9c. Has your child's chest sounded wheezy or whistling apart from colds?

- 1• Yes
2• No

9d. During what month and year did your child's chest first sound wheezy or whistling?

____|____| months (enter calendar month, Jan = 01; Feb = 02); ____|____| Year

9e. Since our last contact with you, **on average**, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say...(e.1)

- 1 Never
2 Twice a week or less
3 More than two times a week, but not every day
4 Everyday, but *not* all the time
5 Everyday, all the time

The Nighttime? Would you say...(e.2)

- 1 Never
2 Once every two weeks or less
3 Once a week
4 Two or three times a week
5 More than three nights a week/Frequently

9f. Since our last contact with you, **during the worst 2 week period**, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say...(f.1)

- 1 Never
2 Twice a week or less
3 More than two times a week, but not every day
4 Everyday, but *not* all the time
5 Everyday, all the time

The Nighttime? Would you say...(f.2)

- 1 Never
2 Once every two weeks or less
3 Once a week
4 Two or three times a week
5 More than three nights a week/Frequently

9g. Since our last contact with you, has your been diagnosed with wheezing by a doctor?

- 1• Yes
2• No

10. Since our last contact with you, has your child had a cough for more than 3 days when he/she did not have a cold?

- 1• Yes 2• No *Skip to Question 11*

IF YES TO QUESTION 10

10a. At what time of the day has this cough usually occurred? (CHECK ALL THAT APPLY)	
1• In the morning, shortly after rising	
2• Later in the day	
3• During the night	
4• No relation to time of day	
10b. Has he/she coughed on most days for as much as 2 to 3 months?	
1• Yes	
2• No	
10c. During what month and year did your child first develop the cough?	
_ _ months (enter calendar month, Jan = 01; Feb = 02);	_ _ Year
10d. Has your child's chest ever sounded wheezy or whistling with episodes of coughing?	
1• Yes	
2• No	
10e. Since our last contact with you, on average , how often has your child had coughing during:	
<u>The Daytime? Would you say... (e.1)</u>	<u>The Nighttime? Would you say... (e.2)</u>
1 <input type="checkbox"/> Never	1 <input type="checkbox"/> Never
2 <input type="checkbox"/> Twice a week or less	2 <input type="checkbox"/> Once every two weeks or less
3 <input type="checkbox"/> More than two times a week, but not every day	3 <input type="checkbox"/> Once a week
4 <input type="checkbox"/> Everyday, but <i>not</i> all the time	4 <input type="checkbox"/> Two or three times a week
5 <input type="checkbox"/> Everyday, all the time	5 <input type="checkbox"/> More than three nights a week/Frequently
10f. Since our last contact with you, during the worst 2-week period , how often has your child had coughing?	
<u>The Daytime? Would you say... (f.1)</u>	<u>The Nighttime? Would you say... (f.2)</u>
1 <input type="checkbox"/> Never	1 <input type="checkbox"/> Never
2 <input type="checkbox"/> Twice a week or less	2 <input type="checkbox"/> Once every two weeks or less
3 <input type="checkbox"/> More than two times a week, but not every day	3 <input type="checkbox"/> Once a week
4 <input type="checkbox"/> Everyday, but <i>not</i> all the time	4 <input type="checkbox"/> Two or three nights a week
5 <input type="checkbox"/> Everyday, all the time	5 <input type="checkbox"/> More than three nights a week/Frequently

11. Since our last contact with you, **on average**, how many **days per month** did you have to change your daytime or evening plans because of your child's breathing problems:

- 1 None, we never had to change plans
2 More than none but less than 3 days
3 3-6 days
4 7 or more days

12. Since our last contact with you, **during the worst 2 week period**, how many **days** did you have to change your daytime or evening plans because of your child's breathing problems:

- 1 None, we never had to change plans
2 More than none but less than 3 days
3 3-6 days
4 7 or more days

13. Since our last contact with you, has your child had asthma, reactive airways disease or a BPD* flare-up diagnosed by a doctor? 1• Yes 2• No

**See Manual for explanation*

14. Since our last contact with you, has your child had bronchiolitis, bronchitis, or pneumonia diagnosed by a doctor?
1• Yes 2• No
15. Since our last contact with you, has your child had croup diagnosed by a doctor?
1• Yes 2• No

The next question are about your baby's diet.

16. Since our last contact with you, did your baby receive mother's breast milk, either at breast, from a bottle or through a tube?
1• Yes 2• No *If NO, skip to Question 17*

If yes to Question 16: _____

16a. For how many months did your child receive breast milk feedings?
Would you say... 1• Less than 1 month
 2• 1-3 months
 3• 4-6 months

16b. For how many months did your child receive breast milk for more than half of his/her feedings?
Would you say... 1• Less than 1 month
 2• 1-3 months
 3• 4-6 months

The next questions are about smoke exposure.

17. Which one of the following 3 statements best describes the situation regarding smoking in your child's home? *Read all options to the interviewee before recording a response.*
- 1 Smoking is allowed in any common room of the home
2 Smoking is limited to part of the house where the child rarely goes
3 There is no smoking inside at all → 17a. Are there any exceptions to this situation?

1• Yes 2• No *(Skip to Question 18)*

17b. Under what circumstances are the exceptions allowed? SPECIFY:

18. Which one of the following 5 statements best describes the situation regarding smoking in your car? *Read all options to the interviewee before recording a response.*
- 1 Do not have a car
2 Smoking is usually or always allowed
3 Smoking is sometimes allowed
4 Smoking occurs in the car only when the child is not inside
5 There is no smoking inside the car → 18a. Are there any exceptions to this situation?

1• Yes 2• No *(Skip to Question 19)*

18b. Under what circumstances are the exceptions allowed? SPECIFY:

19. How often has the mother or primary care giver smoked since your child was born?
1• Never 2• Occasionally 3• Daily

20. How many people in the child's home smoke? |__|__| people

The next questions are about your home and your babysitter's home or day care.

21. Approximately how many hours per week does your child spend at a babysitter's home or day care?

____ hrs *If 0 skip to question 22*

IF 21 is greater than 0: _____

21a. How frequent is there smoke exposure at the babysitter or daycare?

1• Never 2• Occasionally 3• Daily 4• Don't Know

21b. How many children beside your baby are in the daycare? _____ children

22. How many children under 12 live in your house? _____ children

23. Do you have any pets inside the home? 1• Yes 2• No *Skip to Question 24*

23a. If YES, how many pets are there inside the home?

Check all that apply and record number. 1• Dogs _____

2• Cats _____

3• Other _____ SPECIFY: _____

The last questions involve respiratory treatments that your baby may receive.

PROPHYLAXIS

24. Has your child had RSV shots to prevent Respiratory Syncytial Virus (Synagis, palivizumab RSV, shot)?

1• Yes 2• No 3• Don't Know

25. Has your child had a flu shot? 1• Yes 2• No 3• Don't Know

OXYGEN

26. Since our last contact with you, has your child received oxygen therapy at home?

1• Yes 2• No *Skip to Question 27*

If yes to Questions 26 _____

26a. Is your child currently on any oxygen therapy at home?

1• Yes 2• No *Skip to Question 27*

If yes, indicate Yes or No for each

*lpm = liters per minute

26b. Oxygen cannula 1• Yes 2• No FiO2 _____ lpm* _____

26c. Oxygen hood 1• Yes 2• No FiO2 _____ lpm* _____

26d. Ventilator 1• Yes 2• No FiO2 _____ lpm* _____

MEDICATIONS (Enter responses in table. Do not prompt for each medication in the Medication Code List below.)

The next questions involve the medicines your child is taking for breathing problems.

27. Since our last contact with your, what medicines has your baby taken, including medicines taken by a nebulizer or breathing machine at home?	27a. Code	27b. Does he/she take that medicine everyday, sometimes or only when sick? (repeat for each medication)
1		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
2		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
3		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
4		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
5		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
6		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
7		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick

Medication Code List:

<p><i>Rescue medicines:</i></p> <ul style="list-style-type: none"> 1 Albuterol 2 Proventil 3 Serevent 4 Ventolin 5 Volmax 6 Xopenex <p><i>Other Inhaled medications:</i></p> <ul style="list-style-type: none"> 7 Cromolyn (Intal) 8 Nedocromil (Tilade) <p><i>Inhaled steroids:</i></p> <ul style="list-style-type: none"> 9 Advair 10 Aerobid 11 Azmacort 12 Beclovent 13 Flovent 14 Vanceril 15 Pulmicort 	<p><i>Systemic steroids:</i></p> <ul style="list-style-type: none"> 16 Decadron 17 Prednisone 18 Prednisolone <p><i>Leukotriene blocker:</i></p> <ul style="list-style-type: none"> 19 Accolate 20 Singulair <p><i>Methylxanthines:</i></p> <ul style="list-style-type: none"> 21 Theophylline <p><i>Diuretic medications:</i></p> <ul style="list-style-type: none"> 22 Diuril 23 Lasix 24 Aldactizide 25 Aldactone <p><i>Miscellaneous / Non-specific</i></p> <ul style="list-style-type: none"> 26 Nebulizer 27 Other _____
---	--

The next 2 questions are about respiratory infections.....

28. During the past year, for how many days has your child been unable to do his/her usual activities because of illnesses such as chest (not head) colds, bronchitis, asthma or pneumonia?

- 1 0-3 per year
- 2 4-5 per year
- 3 6-9 per year
- 4 more than 9 per year

29. During the past year, how many head colds (common colds) has your child had? Would you say...

- 1 0-3 per year
- 2 4-5 per year
- 3 6-9 per year
- 4 more than 9 per year

The last questions are about allergies.

30. Has your child ever had hay fever or any other condition that makes his/her nose runny, stuffy, or itchy apart from colds? 1 • Yes 2 • No

31. Has your child ever had allergies which cause nose, eye or lung problems?

- 1 • Yes 2 • No

32. Has your child ever been allergic to any food?

- 1 • Yes 2 • No

33. Has he/she ever been allergic to any medicine?

1• Yes 2• No

34. Has your child ever had eczema (allergic skin rash)?

1• Yes 2• No *(End of Interview)*

34a. Was eczema diagnosed by a doctor?

1• Yes 2• No

End of Interview

THANK YOU FOR YOUR COOPERATION

NICU Network

SUPPORT TRIAL
Breathing Outcomes Study

SUPF00 Rel 1.0
December 12, 2005

ENROLLMENT LOG

Center No: Site:

Page 1 of

To be filled out for all infants enrolled in the SUPPORT Trial.

Child's Name Last First	Date of Birth Month/Day/Year	Mother's Initials (optional)	Birth No*	Network Number	Follow-up Number	Consent Granted			Comments
						1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	
	___/___/___	___	___	___	___	1=Yes	2=No	3=Refused	

*Leave blank for a single birth; Enter 1, 2, etc for multiple birth

Initials of person completing this form. _____

NICU Discharge-Baseline Interview

This interview should be administered by trained study staff to the parent/guardian. The target window for this interview is prior to NICU discharge or within the first 30 days following NICU discharge. For patients enrolled in the Pulmonary Outcomes Follow up Study after this target window, this interview should be performed at the time of enrollment.

This interview is for:

_____ (Child's name)

All questions pertain only to his/her health.

N.B. Parents or guardians expressing concerns regarding their child's breathing should be advised to discuss them with the family's primary care physician.

Introduction to the Study:

Premature babies are more likely than full term babies to have breathing problems after discharge from the NICU. The purpose of this study is to see whether or not the treatment your baby received as part of the SUPPORT Study improves your baby's breathing in the 18-22 months following the baby's due date.

As part of this study, we will contact you every 6 months or so to ask you questions about your baby's breathing. The questions will be about your baby's breathing symptoms, especially wheezing and coughing, and about your baby's need for medical visits and treatments for breathing problems.

Wheezing can mean different sounds to different people. By wheezing we mean an expiratory sound (a sound that is made when breathing out, not in) that comes from the chest, sometimes described as whistling or musical.

We have prepared a brochure for you that describes the study and outlines important characteristics of your baby's breathing, especially breathing problems and treatments.

Give brochure

When we call, we'd like you to gather any notes, medications or other information about your baby's breathing. We will ask questions about how often your baby has wheezing or coughing, whether your baby visited a doctor's office, emergency room or was hospitalized for breathing problems, and whether your baby has needed breathing medicines or treatments. If you wish, you may use the brochure to make notes about your baby's breathing.

In order to help us understand your baby's breathing and risk for breathing problems at home, we'd like to ask you a few questions about your home and about whether breathing problems run in the family. As with all information we collect, the answers to these questions will be kept confidential.

Interview Outcome

Was the interview conducted? 1 Yes 2 No

If No why? 1 Loss of contact 2 Interviewee refused 3 Child died 4 Other SPECIFY _____

Initials of person completing this form. ____

1. Child's Name _____ (first) _____ (last) 2. Today's Date: |__|_| - |__|_| - |__|_|_|_|_|
mm dd yyyy

3. Child's Sex: 1 Male 2 Female

4. Child's Birthdate: |__|_| - |__|_| - |__|_|_|_|_|
mm dd yyyy

Enter name and relationship code of the person being interviewed.

5a. Name: _____ 5b. Relationship Code: |__|_|_|

001 - Mother of Child
002 - Father of Child
301 - Adoptive mother
302 - Adoptive father

Other: _____
Common codes are listed here. For other relationships, please look up relationship code from Appendix D of the Breathing Outcomes Manual of Operations and enter above.

6. Type of Interview: 1 Face to Face 2 Telephone

At this time, we would like a little information about the environment in which your new child will grow up.

7. First, how many people normally live with you in your home for at least 6 months of the year?

Total household members: |__|_|

8. After the first few months, will your child be sharing a room with other family members on a regular basis?

1 Yes 2 No

8a. IF YES: How many other people will sleep in the same room with him/her? |__|_|

9. How many rooms are there in your house, excluding closets and bathrooms? |__|_|

10. Do you have any pets inside the home? 1 Yes 2 No Skip to Question 11

If YES, how many.....
10a. check and record number: 1 Dogs in the home? |__|_|
2 Cats in the home? |__|_|
3 Other pets are in the home? |__|_| SPECIFY: _____

11. Does your home or apartment have air conditioning or some kind of cooling where the baby will sleep at night?

1 Yes 2 No Skip to Question 12

If YES,
11a. Air Conditioning? 1 Yes 2 No
11b. Evaporative Cooling? 1 Yes 2 No
(Desert Southwest)
11c. Other? 1 Yes 2 No If YES, SPECIFY _____

12. How is your home heated? (IF MORE THAN ONE, PLEASE CHECK ALL THAT APPLY).

- 1 Steam or hot water (radiator)
2 Central gas furnace (furnace)
3 Electric
4 Wood Stove
5 Other SPECIFY: _____
6 Don't Know

13. What one fuel is used *most* for cooking in your home?

- 1 Electricity
2 Gas
3 Fuel Oil
4 Wood Stove
5 Other SPECIFY: _____
6 Don't Know

The next questions are about your baby's diet.

14. Is your child receiving: (READ ALL CHOICES)

- 1 Only breast milk
2 Only formula (*Skip to Question 15*)
3 Both breast milk and formula (*Skip to Question 15*)
4 Other SPECIFY: _____ (*Skip to Question 15*)

If answer to 14 is 1 (only breast milk)

14a. Will this be supplemented with formula in the first 6 months?

- 1 Yes 2 No 3 Don't Know

14b. If yes, when will supplements begin? |__|__| months

15. Does the mother (you) plan to work outside the home within the next year?

- 1 Yes
2 No
3 Don't Know

The next questions are about smoke exposure.

16. Which one of the following 3 statements best describes the situation regarding smoking in your child's home? *Read all options to the interviewee before recording a response.*

- 1 Smoking is allowed in any common room of the home
2 Smoking is limited to part of the house where the child rarely goes
3 There is no smoking inside at all → 16a. Are there any exceptions to this situation?
1 Yes 2 No (*Skip to Question 17*)

16b. Under what circumstances are the exceptions allowed? SPECIFY:

17. Which one of the following 5 statements best describes the situation regarding smoking in your car? *Read all options to the interviewee before recording a response.*

- 1 Do not have a car
- 2 Smoking is usually or always allowed
- 3 Smoking is sometimes allowed
- 4 Smoking occurs in the car only when the child is not inside
- 5 There is no smoking inside the car → 17a. Are there any exceptions to this situation?
 1 Yes 2 No (*Skip to Question 18*)

17b. Under what circumstances are the exceptions allowed? SPECIFY:

18. How often has the baby's mother or primary caretaker (you) smoked since your child was born?
 1 Never 2 Occasionally 3 Daily

19. Altogether, how many people who live in the child's home smoke? [] [] people

In the next section, we'd like to know what breathing and allergy problems run in the family. Administer attached Family History Questionnaire using the following script:

Mother or guardian:

We'll start with the baby's mother. How old is the baby's biologic mother? Does she have bronchitis, emphysema, COPD, bronchiectasis, asthma, inhaled allergies, or food allergies?

Does the baby's mother have any other chronic respiratory illness?

How often does this person smoke in the baby's home?

Father

For the baby's biologic father, is he living? How old is he? Does he have bronchitis, emphysema, COPD, bronchiectasis, asthma, inhaled allergies, or food allergies?

Does he have any other chronic respiratory illness?

How often does he smoke in the baby's home?

Complete the remainder of the table by collecting the same medical history using the scripting above.

20. Finally, which friend or relative is most likely to be able to contact you 6 months from now in case we lose contact with you?

Name	Relationship
Address	
Telephone	
Cell Phone	
Email	

Thank you for your help in providing us with this important information, and for your continued participation in the Breathing Outcomes Study.

**NICU Discharge-Baseline Interview
Family History Questionnaire**

	Mother	Father	Maternal Grandmother	Maternal Grandfather	Paternal Grandmother	Paternal Grandfather
1. Relationship to enrolled child:						
2. Living?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
3. Age (in years):	_____	_____	_____	_____	_____	_____
4. Does this person have:						
a. COPD	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
b. Chronic Bronchitis?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
c. Emphysema?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
d. Bronchiectasis?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
e. Asthma?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
f. Inhaled Allergies?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
g. Food Allergies?	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK	1.Yes 2.No 3.DK
h. Any other chronic respiratory disease? (SPECIFY)	1.Yes 2.No 3.DK _____	1.Yes 2.No 3.DK _____	1.Yes 2.No 3.DK _____	1.Yes 2.No 3.DK _____	1.Yes 2.No 3.DK _____	1.Yes 2.No 3.DK _____
5. How often does this person smoke in the baby's home*?	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK	1. Never 2. Rarely 3. Sometimes 4. Frequently 5. DK

*Never = never; rarely = less than once per month; sometimes = once per month but less than once /week; frequently = once per week or greater; DK = Don't Know

NICU Network
 SUPPORT TRIAL
 Breathing Outcomes Study
 NICU Discharge-Baseline Interview
 Center: _____ Site: _____ Network No. _____ Follow-up No. _____ Birth No. _____ Mother's Initials: _____
 SUPP01 RA 1.0
 December 12, 2005
 Page 5 of 5

Administered At 6 And 12 Months Corrected Age

This interview should be administered by a trained study interviewer for:

(Child's name)

All questions pertain only to his/her health.

The parent or care giver, who completed the initial interview, should complete this survey and all future surveys. The interviewer will need to ask for that parent (see Manual of Operations).

Introduction Script:

When parent or primary care giver is on phone:

Hello, my name is <your name>. I am calling from the <NICHD Center>. As you probably remember, when you were in the NICU you enrolled in our study about respiratory health of premature infants. I am calling to ask you some questions about your baby's breathing. It will take about 10-20 minutes to complete. Is this a good time for you?

As with all information we collect, the answers to these questions will be kept confidential.

Before we begin this interview, it would be helpful if you could gather any notes you have about your baby's breathing as well as any medications your child has been prescribed or has been taking and have them in front of you. As with all information we collect, the answers to these questions will be kept confidential.

Interview Outcome

Was the interview conducted? 1 Yes 2 No

If No why? 1 Loss of contact 2 Interviewee refused 3 Child died 4 Other SPECIFY _____

Initials of person completing this form. _____

Type of Interview 1 6 Month 2 12 Month

Center: _____ Site: _____ Network No. _____ Follow-up No. _____ Birth No. _____ Mother's Initials: _____ Page 2 of 8

1. TODAY'S DATE: |__|_| - |__|_| - |__|_|_|_|_|
mm dd yyyy

PLEASE CONFIRM PERSONAL INFORMATION AND MAKE NECESSARY CORRECTIONS.

Child's Name: _____
(first) (last)

Child's Birthdate: |__|_| - |__|_| - |__|_|_|_|_|
mm dd yyyy

Telephone Number _____ - _____ - _____

Address _____

Which friend or relative is most likely to be able to contact you 6 months from now in case we lose contact with you?

Name Relationship

Address

Telephone

Cell Phone

Email

Enter name and relationship code of the person being interviewed:

2a. Name: _____ 2b. Relationship Code: |__|_|_|

- 001 - Mother of Child
- 002 - Father of Child
- 301 - Adoptive mother
- 302 - Adoptive father
- Other: _____

Center: _____ Site: _____ Network No. _____ Follow-up No. _____ Birth No. _____ Mother's Initials: _____ Page 3 of 8

3. Type of Interview: 1 Face to Face 2 Telephone4. Location of Interviewer: 1 Local Center
(Option 1) 2 Rochester
(Option 2)**Instructions:**

Parents or guardians expressing concerns regarding their child's breathing should be advised to discuss them with the family's primary care physician.

Where the phrase "last contact" is used below, please substitute with the most specific relevant time prompt, e.g. for the 6 month interview, refer to "since NICU discharge"; for the 12 month interview, refer to "over the past 6 months", etc.

Interview begins:

Some of these questions will be familiar to you. Since we last spoke (__) months ago on (__ / __ / __) we want to learn what changes, if any, there have been to your child's health. We are especially interested in any breathing problems your child may have.

5. Has the child been with you during the past 6 months? 1 Yes 2 No***Since our last contact with you about your child.....***

6. How many times has your child visited a doctor's office? |__|__| times

6a. How many of these times were because of wheezing or breathing problems? |__|__| times

Since our last contact with you about your child.....

7. How many times has your child visited an Emergency Department (Emergency room)? |__|__| times

7a. How many of these times were because of wheezing or breathing problems? |__|__| times

Since our last contact with you about your child.....

8. How many times has your child stayed in the hospital for one or more nights in a row? |__|__| times

8a. How many of these times were because of wheezing or breathing problems? |__|__| times

The next questions are about your baby's breathing.

The first question is about wheezing. By wheezing we mean an expiratory sound (a sound that is made when breathing out, not in) that comes from the chest, sometimes described as whistling or musical.

9. Since our last contact with you, has your baby's chest sounded wheezy or whistling?

- 1 Yes 2 No 3 Don't Know Ask Question 9a for all responses

9a. "Has your baby's breathing sounded like this?" (*play audio clip of wheezing*).

- 1 Yes 2 No 3 Don't Know

IF YES TO QUESTION 9 or 9a:

9b. Has this occurred with colds?

- 1 Yes
2 No
3 Sometimes

9c. Has your child's chest sounded wheezy or whistling apart from colds?

- 1 Yes
2 No

9d. During what month did your child's chest first sound wheezy or whistling?

____ months (enter calendar month, Jan = 01; Feb = 02); ____ Year

9e. Since our last contact with you, **on average**, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say...(e.1)

- 1 Never
2 Twice a week or less
3 More than two times a week, but not every day
4 Everyday, but *not* all the time
5 Everyday, all the time

The Nighttime? Would you say...(e.2)

- 1 Never
2 Once every two weeks or less
3 Once a week
4 Two or three times a week
5 More than three nights a week/Frequently

9f. Since our last contact with you, **during the worst 2 week period**, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say...(f.1)

- 1 Never
2 Twice a week or less
3 More than two times a week, but not every day
4 Everyday, but *not* all the time
5 Everyday, all the time

The Nighttime? Would you say...(f.2)

- 1 Never
2 Once every two weeks or less
3 Once a week
4 Two or three times a week
5 More than three nights a week/Frequently

9g. Since our last contact with you, has your child been diagnosed with wheezing by a doctor?

- 1 Yes
2 No

IF YES, BE SURE TO COMPLETE QUESTION 27

10. Since our last contact with you, has your child had a cough for more than 3 days when he/she did not have a cold?

- 1 Yes 2 No *If NO, skip to Question 11*

IF YES TO QUESTION 10

- 10a. At what time of the day has this cough usually occurred?
(CHECK ALL THAT APPLY)
- 1 In the morning, shortly after rising
2 Later in the day
3 During the night
4 No relation to time of day
- 10b. Has he/she coughed on most days for as much as 2 to 3 months?
1 Yes
2 No
- 10c. During what month and year did your child first develop the cough?
 |_|_| months (enter calendar month, Jan = 01; Feb = 02); |_|_| Year
- 10d. Has your child's chest ever sounded wheezy or whistling with episodes of coughing?
1 Yes
2 No
- 10e. Since our last contact with you, **on average**, how often has your child had coughing during:
The Daytime? Would you say... (e.1) *The Nighttime? Would you say... (e.2)*
- | | |
|--|---|
| 1 <input type="checkbox"/> Never | 1 <input type="checkbox"/> Never |
| 2 <input type="checkbox"/> Twice a week or less | 2 <input type="checkbox"/> Once every two weeks or less |
| 3 <input type="checkbox"/> More than two times a week, but not every day | 3 <input type="checkbox"/> Once a week |
| 4 <input type="checkbox"/> Everyday, but <i>not</i> all the time | 4 <input type="checkbox"/> Two or three times a week |
| 5 <input type="checkbox"/> Everyday, all the time | 5 <input type="checkbox"/> More than three nights a week/Frequently |
- 10f. Since our last contact with you, **during the worst 2-week period**, how often has your child had coughing?
The Daytime? Would you say... (f.1) *The Nighttime? Would you say... (f.2)*
- | | |
|--|---|
| 1 <input type="checkbox"/> Never | 1 <input type="checkbox"/> Never |
| 2 <input type="checkbox"/> Twice a week or less | 2 <input type="checkbox"/> Once every two weeks or less |
| 3 <input type="checkbox"/> More than two times a week, but not every day | 3 <input type="checkbox"/> Once a week |
| 4 <input type="checkbox"/> Everyday, but <i>not</i> all the time | 4 <input type="checkbox"/> Two or three times a week |
| 5 <input type="checkbox"/> Everyday, all the time | 5 <input type="checkbox"/> More than three nights a week/Frequently |

11. Since our last contact with you, **on average**, how many **days per month** did you have to change your daytime or evening plans because of your child's breathing problems:

- 1 None, we never had to change plans
2 More than none but less than 3 days
3 3-6 days
4 7 or more days

12. Since our last contact with you, **during the worst 2 week period**, how many **days** did you have to change your daytime or evening plans because of your child's breathing problems:

- 1 None, we never had to change plans
2 More than none but less than 3 days
3 3-6 days
4 7 or more days

13. Since our last contact with you, has your child had asthma, reactive airways disease or a BPD* flare-up diagnosed by a doctor? 1 Yes 2 No

*See Manual for explanation

14. Since our last contact with you, has your child had bronchiolitis, bronchitis, or pneumonia diagnosed by a doctor?
1 Yes 2 No
15. Since our last contact with you, has your child had croup diagnosed by a doctor?
1 Yes 2 No

The next questions are about your baby's diet.

16. Since our last contact with you, did your baby receive breast milk, either at breast, from a bottle or through a tube?
1 Yes 2 No *If NO, skip to Question 17*

If yes to Question 16:

16a. For how many months did your child receive breast milk feedings?

- Would you say... 1 Less than 1 month
2 1-3 months
3 4-6 months

16b. For how many months did your child receive breast milk for more than half of his/her feedings?

- Would you say... 1 Less than 1 month
2 1-3 months
3 4-6 months

The next questions are about smoke exposure.

17. Which one of the following 3 statements best describes the situation regarding smoking in your child's **home**? *Read all options to the interviewee before recording a response.*

- 1 Smoking is allowed in any common room of the home
2 Smoking is limited to part of the house where the child rarely goes
3 There is no smoking inside at all → 17a. Are there any exceptions to this situation?
1 Yes 2 No (*Skip to Question 18*)

17b. Under what circumstances are the exceptions allowed? SPECIFY:

18. Which one of the following 5 statements best describe the situation regarding smoking in your **car**? *Read all options to the interviewee before recording a response.*

- 1 Do not have a car
2 Smoking is usually or always allowed
3 Smoking is sometimes allowed
4 Smoking occurs in the car only when the child is not inside
5 There is no smoking inside the car → 18a. Are there any exceptions to this situation?
1 Yes 2 No (*Skip to Question 19*)

18b. Under what circumstances are the exceptions allowed? SPECIFY:

19. How often has the **mother or primary care giver** smoked since your child was born?

- 1 Never 2 Occasionally 3 Daily

20. How many people in the child's home smoke? |__|__| people

The next questions are about your home and your babysitter's home or day care.

21. Approximately how many hours per week does your child spend at a babysitter's home or day care?

|_|_| hrs *If 0, skip to Question 22*

IF 21 is greater than 0: _____

21a. How frequent is there smoke exposure at the babysitter or daycare?

1 Never 2 Occasionally 3 Daily 4 Don't Know

21b. How many children beside your baby are in the daycare? |_|_| children

22. How many children under 12 live in your house? |_|_| children (including the baby)

23. Do you have any pets inside the home? 1 Yes 2 No *Skip to Question 24*

23a. If YES, how many pets are there inside the home?

Check all that apply and record number: 1 Dogs |_|_|2 Cats |_|_|3 Other |_|_| SPECIFY: _____**The last questions involve respiratory treatments that your baby may receive.****PROPHYLAXIS**

24. Has your child had RSV shots to prevent Respiratory Syncytial Virus (Synagis, palivizumab, RSV shot)?

1 Yes 2 No 3 Don't Know25. Has your child had a flu shot? 1 Yes 2 No 3 Don't Know**OXYGEN**

26. Since our last contact with you, has your child received oxygen therapy at home?

1 Yes 2 No *Skip to Question 27*

If yes to Questions 26 _____

26a. Is your child currently on any oxygen therapy at home?

1 Yes 2 No *Skip to Question 27*

If yes, indicate Yes or No for each

*lpm = liters per minute

26b. Oxygen cannula 1 Yes 2 No FiO2 _____ lpm* _____26c. Oxygen hood 1 Yes 2 No FiO2 _____ lpm* _____26d. Ventilator 1 Yes 2 No FiO2 _____ lpm* _____

Center: _____ Site: _____ Network No. _____ Follow-up No. _____ Birth No. _____ Mother's Initials: _____ Page 8 of 8

MEDICATIONS (Enter responses in table. Do not prompt for each medication in the Medication Code List below.)**The last two questions involve the medicines your child is taking for breathing problems.**

27. Since our last contact with you, what medicines has your baby taken, including medicines delivered by a nebulizer or breathing machine at home?	27a. Code	27b. Does he/she take that medicine everyday, sometimes or only when sick? (repeat for each medication)
1		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
2		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
3		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
4		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
5		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
6		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick
7		<input type="checkbox"/> Everyday <input type="checkbox"/> Sometimes <input type="checkbox"/> Only when Sick

Medication Code List:

Rescue medicines: 1 Albuterol 2 Proventil 3 Serevent 4 Ventolin 5 Volmax 6 Xopenex Other Inhaled medications: 7 Cromolyn (Intal) 8 Nedocromil (Tilade) Inhaled steroids: 9 Advair 10 Aerobid 11 Azmacort 12 Beclovent 13 Flovent 14 Vancericil 15 Pulmicort	Systemic steroids: 16 Decadron 17 Prednisone 18 Prednisolone Leukotriene blocker: 19 Accolate 20 Singulair Methylxanthines: 21 Theophylline Diuretic medications: 22 Diuril 23 Lasix 24 Aldactizide 25 Aldactone Miscellaneous / Non-specific 26 Nebulizer 27 Other _____
---	--

Thank you for your cooperation in providing us with this important information, and for your continued participation in the Breathing Outcomes Study.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "nfiner@ucsd.edu"; "wcarlo@peds.uab.edu"
Subject: Re: ATS
Date: Friday, May 07, 2010 10:07:06 AM

This is fine
Rose

----- Original Message -----

From: Finer, Neil <nfiner@ucsd.edu>
To: Wally Carlo, M.D. <WCarlo@peds.uab.edu>; Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri May 07 09:45:00 2010
Subject: RE: ATS

Hi Wally and Rose
I can send John both the presentations if its OK with you
Neil

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Friday, May 07, 2010 4:50 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil
Subject: RE: ATS

SURE! Did not know that!!!

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, May 07, 2010 6:21 AM
To: Wally Carlo, M.D.; 'nfiner@ucsd.edu'
Subject: Re: ATS

He is the discussant for the session and missed the support presentations at PAS.
Rose

----- Original Message -----

From: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu <nfiner@ucsd.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>
Sent: Fri May 07 06:38:36 2010
Subject: RE: ATS

Ok with me. Why Kinsella? I don't have his email address.

Wally

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>

Sent: Friday, May 07, 2010 12:01 AM

To: 'nfiner@ucsd.edu' <nfiner@ucsd.edu>; 'wcarlo@peds.uab.edu' <wcarlo@peds.uab.edu>

Subject: ATS

Hi,

Neil had asked that the presentations be shared with John Kinsella. As long as this is done confidentially and there is no risk of violating the embargo (i.e. He keeps the info confidential until the day of presentation), this is fine.

Thanks again for all the hard work and effort!

Rose

From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [McGrath, John \(NIH/NICHD\) \[E\]](#); [Miller, Marianne Glass \(NIH/NICHD\) \[E\]](#)
Subject: Final remarks for Preterm oxygen briefing
Date: Thursday, May 06, 2010 6:32:20 PM
Attachments: [Final Rose Higgins Remarks Audio Briefing.docx](#)

Hi all. Attached is the final copy of Rose's remarks for the preterm oxygen studies briefing on the 12th. John and Marianne, these are also in the "Preterm Oxygen Studies" folder in the 2010 releases folder on the N: Drive.

Thanks.

I am Dr. Rosemary Higgins, the Program Scientist for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development's Neonatal Research Network.

The NICHD Neonatal Research Network is made up of 20 academic medical centers from around the US. These centers work together with NICHD to improve the care and health of infants born with medical problems such as infant born prematurely. The network is a cooperative agreement between the medical centers and the national institutes of health, to test treatments for newborn infants. The network was created in 1986 because many of the treatment and management strategies in use at the time had become standards without being evaluated in a research study.

The NICHD Neonatal Research network undertook the current study to investigate management of breathing strategies and oxygen saturation target levels of extremely low birth weight infants. Higher oxygen levels have been linked to an increase in the risk of retinopathy of prematurity (ROP), a condition affecting the retina. The current study was undertaken to determine if slightly reduced oxygen levels would allow infants to remain healthy while reducing their risk for ROP.

Researchers in the NICHD Neonatal Research Network observed more than 1,300 infants born at 20 sites. These infants were very premature—born in the 24th through the 27th week of pregnancy. They weighed only one or two pounds and many needed respiratory therapy. For one portion of our study, we compared outcomes for infants receiving two different oxygen saturation levels. Infants with blood oxygen levels between 85 to 89 percent were compared with infants whose blood oxygen saturation levels were maintained at 91 to 95 percent. The other part of the study compared the methods used to provide oxygen to the infants: ventilator and surfactant versus the CPAP device.

The National Heart Lung and Blood Institute also contribute for support for this study. The investigators from the NICHD NRN will now present our findings.

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Thursday, May 06, 2010 11:47 AM
To: Moskowitz, Deborah
Cc: Higgins, Rosemary (NIH/NICHD) [E]; 'WCarlo@peds.uab.edu'
Subject: RE: NEJM article page proofs

Hello Debbie
Thanks for getting the galleys to me
I have reviewed these and they look OK
There is only one issue – regarding the author line
We would like this to read;

SUPPORT study group (or subcommittee) of the Eunice Kennedy Shriver NICHD Neonatal Research Network.

We have made the same request for the Carlo paper and would ask that the author lines are the same for both papers.

Many thanks for your assistance.
Be well
Neil Finer

From: Moskowitz, Deborah [<mailto:dmoskowitz@nejm.org>]
Sent: Wednesday, May 05, 2010 4:04 PM
To: Finer, Neil
Subject: NEJM article page proofs
Importance: High

Hi, Dr. Finer,

Here are the page proofs of your article (I decided not to wait for Layout to send them out). I can't imagine why you didn't receive them! Let me know how they look to you.

--Debbie

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "nfiner@ucsd.edu"
Subject: Galleys
Date: Thursday, May 06, 2010 11:17:06 AM

Neil

Please be sure that the following language for authorship is used

SUPPORT study group (or subcommittee) of the Eunice Kennedy Shriver NICHD Neonatal Research Network.

We just sent this in for Wally's paper

Thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wcarlo@peds.uab.edu"
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: Fw: Oximtreys galleys
Date: Thursday, May 06, 2010 11:06:06 AM
Attachments: Carlo, SUPPORT, galleys, 2010-05-06 changes.doc

Wally

Here it is. Let us know if you need anything else

Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu May 06 11:04:52 2010
Subject: RE: Oximtreys galleys

Here it is in Word (attached).

In case you can't read it on your Blackberry:

The following changes need to be made in the Acknowledgements:

1. For Brown University, insert after D. Gingras:

S. Barnett; S. Lillie;

2. For Case Western Reserve University, insert after B.S. Siner:

A. Zadell; J. DiFiore.

3. For University of Cincinnati, delete: V. Narendran (he is an author)

4. For Emory University, insert after E.C. Hale:

A. K. Hutchinson;

5. For University of Alabama, delete: N. Ambalavanan (he is an author)

6. For University of Rochester, insert before L.J. Reubens:

G.D. Markowitz;

7. For University of Texas Southwestern (Dallas), insert after N.A. Miller:

J. Allen; L. Grau; M. Martin; A. Solis; D.M. Vasil; K. Wilder.

8. For the Data and Safety Monitoring Committee

a. Columbia University is incorrectly listed as in Rockville, MD. Please change to New York, NY.

b. A. Das is with RTI International, Rockville, MD

c. W.K. Poole is with RTI International, Research Triangle Park, NC

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, May 06, 2010 10:51 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: Oximtrex galleys

Can you send the line by line additions in a WORD document in the next hour? The editorial assistant didn't make the changes with our prior editing attempt on the galleys.

Thanks
Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu May 06 10:20:49 2010
Subject: RE: Oximtrex galleys

The authors are in the correct order, but they did not make all of the requested changes on the boilerplate. See attached with red balloons for changes.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, May 06, 2010 1:41 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Oximtrex galleys
Importance: High

Stephanie

Here are Wally's galleys- can you make sure the authors are in the appropriate order and that the correct individuals are listed in the boilerplate?

Please do this first on THURSDAY and send it back to me.

Also, I will not be in the office until Monday now. I am taking a leave day on Friday.

Rose
Rosemary D. Higgins, MD
Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research
Network
Pregnancy and Perinatology Branch
CDBPM, NIH
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-435-7909
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

Wally,

The following changes need to be made in the Acknowledgements:

1. For Brown University, insert after D. Gingras:

S. Barnett; S. Lillie;

2. For Case Western Reserve University, insert after B.S. Siner:

A. Zadell; J. DiFiore.

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A. K. Hutchinson;

5. For University of Alabama, delete: N. Ambalavanan (he is an author)

6. For University of Rochester, insert before L.J. Reubens:

G.D. Markowitz;

7. For University of Texas Southwestern (Dallas), insert after N.A. Miller:

J. Allen; L. Grau; M. Martin; A. Solis; D.M. Vasil; K. Wilder.

8. For the Data and Safety Monitoring Committee

- a. Columbia University is incorrectly listed as in Rockville, MD. Please change to New York, NY.

- b. A. Das is with RTI International, Rockville, MD

- c. W.K. Poole is with RTI International, Research Triangle Park, NC

From: [Webb, Robin E.](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT data queries
Date: Wednesday, May 05, 2010 2:16:11 PM

Hi Rose,

For this and the protocol, do you want to poll for before the SC meeting? Or start the following week?

Thanks,
Robin

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, May 05, 2010 12:14 PM
To: Webb, Robin E.
Cc: Archer, Stephanie (NIH/NICHD) [E]; Das, Abhik; Zaterka-Baxter, Kristin
Subject: FW: SUPPORT data queries

Robin
Can you send to the SUPPORT subcommittee and set up a call??

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Michael Cotten [<mailto:cotte010@mc.duke.edu>]
Sent: Saturday, May 01, 2010 8:19 PM
To: Neil Finer; Wally Carlo, M.D.
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Ronald N Goldberg
Subject: SUPPORT data queries

Hi Neil and Wally, Rose and Ron...

first..congratulations on the first presentation of results and publication of the manuscripts!!!!

here are two secondary data analysis proposals for SUPPORT,,,,one looking at the DR CPAP portion of the study, the other at the oxygen sat target portion.

thanks

mc

C. Michael Cotten MD MHS
Associate Professor of Pediatrics
Medical Director Neonatology Clinical Research
Duke University Medical Center
Box 2739 DUMC
Durham, NC 27710
2424 Erwin Road Suite 504

Durham, NC 27705
ph: 919-681-6024
fax: 919-681-6065
email: cotte010@mc.duke.edu

From: Pablo Sanchez
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Presentation of NICHD Data
Date: Tuesday, May 04, 2010 11:03:16 AM

Thanks, rose-i really appreciate your doing this-pablo
Pablo -sent from Blackberry
214-648-3753 (office)
214-621-1068 (cell)
972-206-9021 (beeper)

-----Original Message-----

From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
To: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>

Sent: 5/4/2010 8:01:52 AM
Subject: Re: Presentation of NICHD Data

This has been approved by the steering committee

Rose

----- Original Message -----

From: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
Sent: Sat May 01 22:18:10 2010
Subject: Re: Presentation of NICHD Data

Hi Rose and Pablo,

I have attached a file with the slides containing the newer data from the Outcomes Following Delivery Room CPR in ELBW infants study. These data focus on the DR-CPR group and comparing those that had low 5 min Apgar versus those that had improved by 5 minutes. These numbers all came from Doug Kendrick with RTI and he has double checked them multiple times. They are being used in the manuscript. I appreciate your willingness to see if your group would be amenable to having these presented at the Resuscitation Meeting following SPR. I completely understand if it is not possible. Thanks for trying.

Myra

Myra H. Wyckoff, MD
Associate Professor of Pediatrics
UT Southwestern Medical School
214-648-3753

Director, Newborn Resuscitation Services
Parkland Health and Hospital System

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<http://www.utsouthwestern.edu/>)

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 4/30/2010 6:21 PM >>>

Hi

Myra can use the info in the abstract. Items from the paper should not be used to respect the embargo policy

Thanks

Rose

----- Original Message -----

From: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>

To: Higgins, Rosemary (NIH/NICHD) [E]

Cc: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>

Sent: Fri Apr 30 19:10:59 2010

Subject: Fw: Presentation of NICHD Data

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214-621-1068 (cell)

972-206-9021 (beeper)

From: Myra Wyckoff
To: Higgins, Rosemary (NIH/NICHD) [E]; Pablo Sanchez
Subject: Re: Presentation of NICHD Data
Date: Tuesday, May 04, 2010 10:01:52 AM

Thanks so much Rose. I really appreciate your efforts and will not make such an error again.

Sincerely,
Myra

Myra H. Wyckoff, MD
Associate Professor of Pediatrics
UT Southwestern Medical School
214-648-3753

Director, Newborn Resuscitation Services
Parkland Health and Hospital System

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>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 5/4/2010 8:01 AM >>>
This has been approved by the steering committee

Rose

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From: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
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Sent: Sat May 01 22:18:10 2010
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Myra

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Subject: Fw: Presentation of NICHD Data

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Pablo -sent from Blackberry

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972-206-9021 (beeper)

From: Pablo Sanchez
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Presentation of NICHD Data
Date: Sunday, May 02, 2010 3:10:47 AM

Yes-thanks,rose-i appreciate it-pablo

Pablo -sent from Blackberry

214-648-3753 (office)

214-621-1068 (cell)

972-206-9021 (beeper)

-----Original Message-----

From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>
To: Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>
To: bpoindex@iupui.edu <bpoindex@iupui.edu>
To: vanmeurs@leland.stanford.edu <vanmeurs@leland.stanford.edu>
Cc: Stephanie (NIH/NICHD) [E] Archer <archerst@mail.nih.gov>
To: goldb008@mc.duke.edu <goldb008@mc.duke.edu>
To: sshankar@med.wayne.edu <sshankar@med.wayne.edu>
To: barbara_stoll@oz.ped.emory.edu <barbara_stoll@oz.ped.emory.edu>
To: wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>
To: mcw3@po.cwru.edu <mcw3@po.cwru.edu>
To: adas@rti.org <adas@rti.org>
To: kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>
To: ifrantz@tuftsmedicalcenter.org <ifrantz@tuftsmedicalcenter.org>
To: edward-bell@uiowa.edu <edward-bell@uiowa.edu>
To: Kathleen.A.Kennedy@uth.tmc.edu <Kathleen.A.Kennedy@uth.tmc.edu>
To: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
To: alaptook@WIHRI.org <alaptook@WIHRI.org>
To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>

Sent: 5/2/2010 12:06:11 AM

Subject: Fw: Presentation of NICHD Data

Hi

Myra would like to use the attached slides at a post PAS resuscitation meeting. Please send me a yes/no vote by 5/4

Thanks

Rose

----- Original Message -----

From: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
Sent: Sat May 01 22:18:10 2010
Subject: Re: Presentation of NICHD Data

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To: Higgins, Rosemary (NIH/NICHD) [E]
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Subject: Fw: Presentation of NICHD Data

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972-206-9021 (beeper)

From: Myra Wyckoff
To: Higgins, Rosemary (NIH/NICHD) [E]; Pablo Sanchez
Subject: Re: Presentation of NICHD Data
Date: Saturday, May 01, 2010 10:18:37 PM
Attachments: New Data for Preemie CPR Data.pptx

Hi Rose and Pablo,

I have attached a file with the slides containing the newer data from the Outcomes Following Delivery Room CPR in ELBW infants study. These data focus on the DR-CPR group and comparing those that had low 5 min Apgar versus those that had improved by 5 minutes. These numbers all came from Doug Kendrick with RTI and he has double checked them multiple times. They are being used in the manuscript. I appreciate your willingness to see if your group would be amenable to having these presented at the Resuscitation Meeting following SPR. I completely understand if it is not possible. Thanks for trying.

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Rose

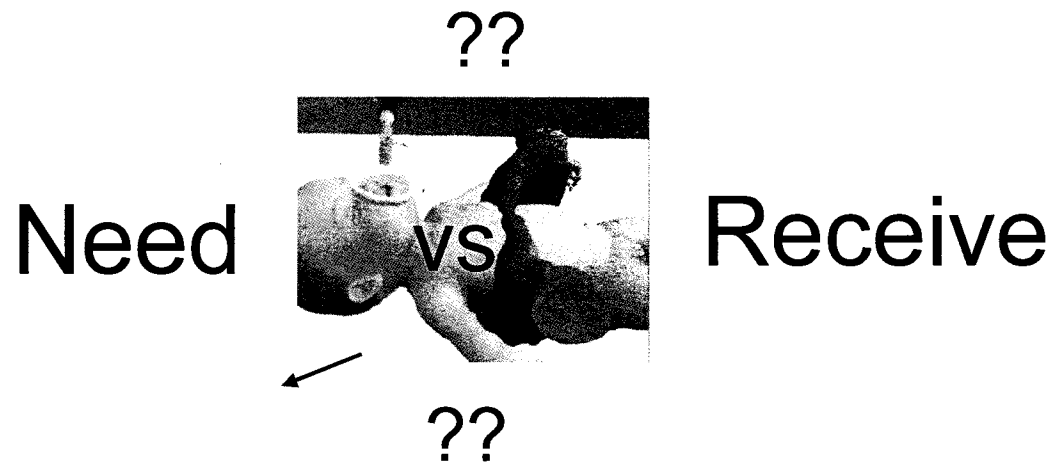
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Cc: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
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Subject: Fw: Presentation of NICHD Data

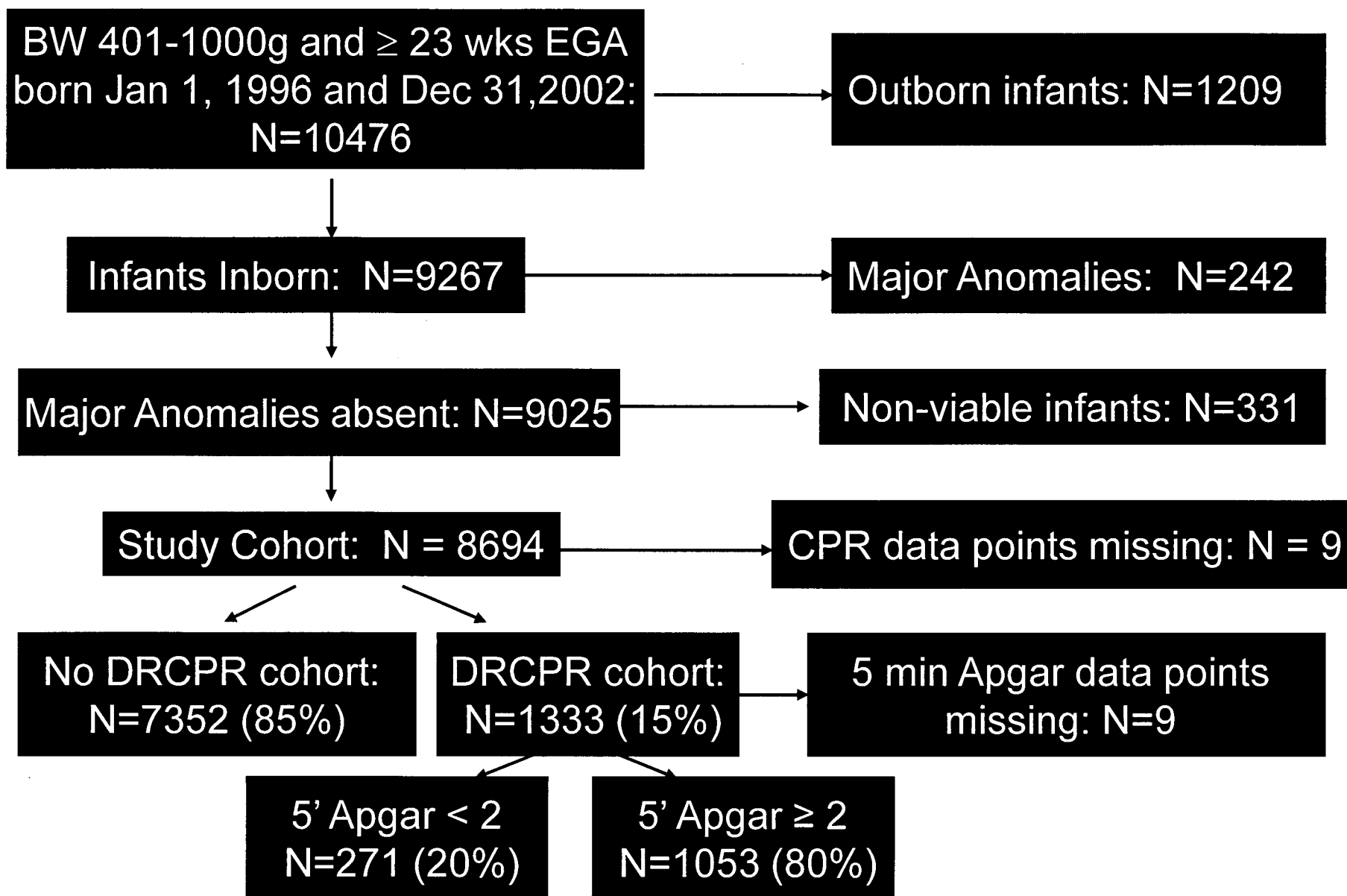
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that it is ok -thanks-pablo
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Did all DR-CPR babies require
CPR in the delivery room or did
they merely receive CPR?



Results: Flow Diagram of the Patient Selection



Perinatal and Demographic Characteristics

	Apgar < 2 (N= 271)	Apgar ≥ 2 (N= 1053)	P
% Multiple birth	23%	24%	ns
% Maternal Hypertension	13%	21%	0.0015
% Antepartum Hemorrhage	24%	20%	ns
% Antenatal Steroids*	35%	46%	0.0025
Mode of delivery			
% vaginal breech	17%	13%	ns
% C section	50%	57%	
Gestational age (wks)	24.9 ± 1.6	25.3 ± 1.6	0.0028
Birth weight (g)	692 ± 142	713 ± 140	0.0262
% SGA	15%	15%	ns
% Males	59%	51%	0.0243

*Complete antenatal steroids within 7 days of delivery

Results: Short Term Outcomes

	Apgar < 2 (n=271))		Apgar ≥ 2 (n= 1053)		P
	N*	%	N*	%	
Death < 12 h	271	44%	1053	8%	<0.0001
% Pneumothorax	152	16%	964	11%	ns
% Pulmonary hemorrhage	152	15%	964	12%	ns
% PDA	152	50%	964	45%	ns
% Grade III & IV IVH	134	34%	850	23%	0.0096
% PVL by 36 weeks	131	10%	838	6%	ns
% NEC Stage 2 or 3	152	7%	962	10%	ns
% Postnatal Steroids	152	46%	964	44%	ns
% BPD (O ₂ at 36 wk)	101	73%	964	56%	0.0007
Hospital Death ≤ 120 d	271	64%	1053	36%	<0.0001

*Number of infants evaluated for each outcome

Results: Long Term Outcomes at 18-22 Mo

	Apgar < 2 (n=271)		Apgar ≥ 2 (n= 1053)		P
	N*	%	N*	%	
Death by 18-22 mo follow-up	271	66%	1052	38%	<0.0001
NDI	71	52%	507	43%	ns
NDI or Death	249	86%	909	68%	<0.0001
MDI < 70	72	44%	514	35%	ns
PDI < 70	68	37%	505	28%	ns
MDI (Mean ± sd)	72	73±19	514	76±18	ns
PDI (Mean ± sd)	68	77±20	505	80±20	ns
Moderate or Severe CP	77	13%	550	10%	ns
Blind in both eyes	77	0.0%	546	0.4%	ns
Hearing Aid in both ears	77	4%	549	3%	ns

*# of infants evaluated for each outcome

92% Follow up rate for NDI and Death

Prognostic Implications of 5' Apgar < 2 on Short Term Outcomes using Logistic Modeling

	Odds Ratio	95% Confidence Interval
Death < 12 h	8.01	5.64 – 11.38
Pulm Hemorrhage	1.21	0.74 – 1.99
Pneumothorax	1.33	0.82 – 2.18
PDA	1.10	0.76 – 1.59
IVH grade 3 or 4	1.57	1.04 – 2.39
NEC	0.69	0.34 – 1.33
BPD	1.79	1.07 – 2.99
Postnatal Steroids	1.03	0.72 – 1.48
Hospital Death \leq 120 d	3.01	2.19 – 4.15

Prognostic Implications of 5' Apgar < 2 on Long Term Outcomes using Logistic Modeling

	Odds Ratio	95% Confidence Interval
Did not complete follow-up	0.43	0.32 – 0.59
NDI	1.67	0.97 – 2.86
Death by 18-22 mo follow-up	2.88	2.09 – 3.96
NDI or Death	2.94	1.93 – 4.49
MDI < 70	1.61	0.95 – 2.74
PDI < 70	1.59	0.90 – 2.78

Conclusions

- ELBW infants who undergo delivery room CPR and have a 5 min Apgar score < 2 have only a 14% chance of disability free survival
- Prolonged CPR in such infants should be viewed with caution.
- Exploration of protective strategies in this high risk population of ELBW infants is needed.

From: Myra Wyckoff
To: Higgins, Rosemary (NIH/NICHD) [E]; Pablo Sanchez
Subject: Re: Presentation of NICHD Data
Date: Saturday, May 01, 2010 12:14:42 AM

Got it. Thanks!
M.

Myra H. Wyckoff, MD
Associate Professor of Pediatrics
UT Southwestern Medical School
214-648-3753

Director, Newborn Resuscitation Services
Parkland Health and Hospital System

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972-206-9021 (beeper)

From: Pablo Sanchez
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: ****SUPPORT MASTEHEADS
Date: Friday, April 30, 2010 11:45:14 PM

Great-makes more sense-pablo
Pablo -sent from Blackberry
214-648-3753 (office)
214-621-1068 (cell)
972-206-9021 (beeper)

-----Original Message-----

From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: william_oh@brown.edu <william_oh@brown.edu>
To: edward.donovan@cchmc.org <edward.donovan@cchmc.org>
To: kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>
To: Bradley.yoder@hsc.utah.edu <Bradley.yoder@hsc.utah.edu>
To: Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>
To: bpoindex@iupui.edu <bpoindex@iupui.edu>
To: vanmeurs@leland.stanford.edu <vanmeurs@leland.stanford.edu>
Cc: Stephanie (NIH/NICHD) [E] Archer <archerst@mail.nih.gov>
To: cotte010@mc.duke.edu <cotte010@mc.duke.edu>
To: goldb008@mc.duke.edu <goldb008@mc.duke.edu>
To: sshankar@med.wayne.edu <sshankar@med.wayne.edu>
To: mcaplan@northshore.org <mcaplan@northshore.org>
To: barbara_stoll@oz.ped.emory.edu <barbara_stoll@oz.ped.emory.edu>
To: wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>
To: aaf2@po.cwru.edu <aaf2@po.cwru.edu>
To: mcw3@po.cwru.edu <mcw3@po.cwru.edu>
To: adas@rti.org <adas@rti.org>
To: dwallace@rti.org <dwallace@rti.org>
Cc: kzaterka@rti.org <kzaterka@rti.org>
Cc: mcunningham@rti.org <mcunningham@rti.org>
To: poo@rti.org <poo@rti.org>
To: kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>
To: dstevenson@stanford.edu <dstevenson@stanford.edu>
To: ifrantz@tuftsmedicalcenter.org <ifrantz@tuftsmedicalcenter.org>
To: ambal@uab.edu <ambal@uab.edu>
To: nfiner@ucsd.edu <nfiner@ucsd.edu>
To: edward-bell@uiowa.edu <edward-bell@uiowa.edu>
To: rohls@unm.edu <rohls@unm.edu>
To: Jon.E.Tyson@uth.tmc.edu <Jon.E.Tyson@uth.tmc.edu>
To: Kathleen.A.Kennedy@uth.tmc.edu <Kathleen.A.Kennedy@uth.tmc.edu>
To: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
To: Luc Brion <Luc.Brion@UTSouthwestern.edu>

Sent: 4/30/2010 9:27:32 AM
Subject: Re: ****SUPPORT MASTEHEADS

Hi

Wally has spoken to NEJM and they are willing to consider adding the authors back to the masthead (with affiliations in the appendix) depending on space.

I will keep folks updated.

Thanks for the feedback

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]

To: (Luc.Brion@UTSouthwestern.edu) <Luc.Brion@UTSouthwestern.edu>; (rohls@unm.edu) <rohls@unm.edu>; aaf2@po.cwru.edu <aaf2@po.cwru.edu>; Abhik Das <adas@rti.org>; alaptook@WIHRI.org <alaptook@WIHRI.org>; Ambal (ambal@uab.edu) <ambal@uab.edu>; Brad Yoder (Bradley.yoder@hsc.utah.edu) <Bradley.yoder@hsc.utah.edu>; Brenda Poindexter <bpoindex@iupui.edu>; Carlo Waldemar (E-mail) <wcarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; Dennis Wallace <dwallace@rti.org>; Ed Bell <Edward-bell@uiowa.edu>; Ed Donovan <edward.donovan@cchmc.org>; Ehrenkranz Richard (E-mail) <richard.ehrenkranz@yale.edu>; Ivan Frantz (ifrantz@tuftsmedicalcenter.org) <ifrantz@tuftsmedicalcenter.org>; Kennedy, Kathleen A <Kathleen.A.Kennedy@uth.tmc.edu>; Kristi Watterberg <kwatterberg@salud.unm.edu>; Kurt Schibler [kurt.schibler@cchmc.org] <kurt.schibler@cchmc.org>; Matthew Bizzarro <matthew.bizzarro@yale.edu>; Michelle Walsh <mcw3@po.cwru.edu>; Mickey Caplan <mcaplan@northshore.org>; Oh William (E-mail) <william_oh@brown.edu>; Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>; Poole Kenneth (E-mail) <poo@rti.org>; Roger Faix <Roger.Faix@hsc.utah.edu>; Ronald GOldberg <goldb008@mc.duke.edu>; Seetha Shankaran <sshankar@med.wayne.edu>; Stevenson David (E-mail) <dstevenson@stanford.edu>; Stoll Barbara (E-mail) <barbara_stoll@oz.ped.emory.edu>; Tyson Jon (E-mail) <Jon.E.Tyson@uth.tmc.edu>; VanMeurs, Krisa <vanmeurs@leland.stanford.edu>

Cc: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg <mcunningham@rti.org>; kristin zaterka <kzaterka@rti.org>

Sent: Thu Apr 29 15:01:20 2010

Subject: ****SUPPORT MASTEHEADS

HI,

Due to space limitations for the two SUPPORT papers, NEJM has requested to list the authorship as NICHD NRN and SUPPORT Study Group. Bothe Neil and Wally are ok with this and authors will be recognized on PubMed.

Rose

From: Hogan, Sharon [mailto:shogan@nejm.org]

Sent: Thursday, April 29, 2010 9:13 AM

To: 'Wally Carlo, M.D.'; Finer, Neil

Cc: Moskowitz, Deborah

Subject: RE: Your articles in the NEJM

Hello again,

We are still having difficulty fitting the list of authors, the authors' affiliations, and the abstract on the first page of each of these articles. We would like to simply list "The NICHD Neonatal Research Network and the SUPPORT Study Group" under the title and then move the list of authors and affiliations to the Appendix.

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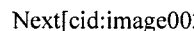
Volume 362:1477-1490

[cid:image001.gif@01CAE7AC.DC06E130]

April 22, 2010 <<http://content.nejm.org/content/vol362/issue16/index.dtl>>

[cid:image001.gif@01CAE7AC.DC06E130]

Number 16

Next[cid:image002.gif@01CAE7AC.DC06E130]<<http://content.nejm.org/cgi/content/short/362/16/1491?query=nextarrow>>

Effect of Valsartan on the Incidence of Diabetes and Cardiovascular Events
The NAVIGATOR Study Group

Please confirm that these changes would be okay.

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: [Pablo Sanchez](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [Myra Wyckoff](#)
Subject: Fw: Presentation of NICHD Data
Date: Friday, April 30, 2010 7:11:25 PM
Attachments: [Presentation of NICHD Data.msg](#)

Hi rose-see below-myra is presenting a talk at a resusc meeting after pas and she will use some of the data from an abstract that was presented previously and the manuscript that has been sent out to co-authors-wanted to be sure that it is ok -thanks-pablo

Pablo -sent from Blackberry

214-648-3753 (office)

214-621-1068 (cell)

972-206-9021 (beeper)

Blansfield, Earl (NIH/NICHD) [E]

From: Myra Wyckoff <Myra.Wyckoff@UTSouthwestern.edu>
Sent: Friday, April 30, 2010 6:24 PM
To: Pablo Sanchez
Subject: Presentation of NICHD Data
Attachments: Program.pdf

Pablo,

Thanks for much for making me aware of the need to get permission to present the study entitled "Outcome of Extremely Low Birth Weight Infants Receiving Delivery Room Cardiopulmonary Resuscitation" Authors: Myra H. Wyckoff, MD, Walid A. Salhab, MD Roy J. Heyne, MD, Douglas E. Kendrick, Abbot R. Laptook, MD, For the NICHD Neonatal Research Network NICHD which I was going to present at the 2nd Neonatal Resuscitation Research Workshop in Vancouver, CA May 5-6 (see attached program). This is a symposium of about 50 people who are involed in newborn resuscitation research from various aspects. The presentations are 10 minute talks with 5 minutes of discussion. It makes sense that I would need permission and I apologize for not thinking of this issue before. I would appreciate it if you could help me with contacting the appropriate people for permission. If it can't be done then I am sure I can find something else to present. Let me know and thanks for your help.

Myra

9:00 – 9:20 am
Jane Pillow
Reflex during establishment of ventilation

9:20 – 9:40 am
Masanori Tamura
Different ways of a tracheal suction to prevent MAS

9:40 – 10:00 am
MORNING TEA – Quarter Deck and Bridge

10:00 – 10:20 am (Chairperson: John Kattwinkel)
Susan Niermeyer
Field testing of global educational program for neonatal resuscitation.

10:20 – 10:40 am
Ruth Guinsburg
Deaths up to 6 days after birth associated with intrauterine hypoxia or asphyxia in Brazil: a 2005-2007 national study.

10:40 – 11:00 am
Rosemary Higgins
Challenges and opportunities for research in the Neonatal Research Network.

11:00 – 11:20 am
Maria Fernanda Branc de Almeida
Hypothermia in preterm newborn infants <34 weeks born in the Brazilian Neonatal Network: a prospective study from delivery room to NICU admission.

11:20 – 11:40 am
Brett Manley
Clinical assessment of extremely premature infants in the delivery room as a poor predictor of survival

11:40 – 12:30 pm
LUNCH – Dockside Restaurant

12:30 – 12:50 pm (Chairperson: Myra Wyckoff)
Stuart Hooper
Cardiovascular transition at birth and the potential benefit of delayed cord clamping

1:00 – 1:40 pm
Haïd Aziz
Practical application of delayed cord clamping

1:10 – 1:30 pm
Marilyn Escobedo
Echocardiographic studies in transitional circulation.

1:30 – 1:50 pm
Michael Meyer
SVC flow and cord clamping.

1:50 – 2:10 pm
AFTERNOON TEA – Quarter Deck and Bridge

2:10 – 2:30 pm (Chairperson: Susan Niermeyer)
Lou Halamek
Value of simulation and debriefing in neonatal resuscitation.

2:30 – 2:50 pm
Wade Rich
The problems of antenatal consent in delivery room RCTs.

2:50 – 3:10 pm
Myra Wyckoff
Impact of delivery room CPR on the outcome of preterm infants.

3:10 – 3:30 pm
Anne Lee Solevag
What is the optimal compression ventilation ratio?

3:30 – 3:50 pm
Late Afternoon Tea – Quarter Deck and Bridge

3:50 – 4:10 pm
Ingrid Dannevig
Can the number of newborns receiving cardiac compressions be reduced?

4:10 – 4:30
Colin Morley
Personal views of 40 years of neonatal resuscitation.

4:30 – 4:40 pm
Alan Jobe
Send us away wiser.

7:30 pm
DINNER – Dockside Restaurant

2nd Neonatal Resuscitation

Research Workshop

4th - 6th May 2011



Quarter Deck and
Bridge Rooms

The Granville Island Hotel
1253 Johnston Street
Vancouver, BC

Canada

Fisher & Paykel HEALTHCARE MASIMO
Dräger

Tuesday 4th May

7.30 pm Welcome Dinner
Dockside Restaurant
The Granville Island Hotel

Wednesday 5th May

8.00 – 8.10 am (Chairperson: Richard Martin)
Colin Morley
Welcome and why are we here?

8.10 – 8.30 am
Ola Saugstad
Metabolomic analyses of plasma. New insights into asphyxia and resuscitation in pigs.

8.30 – 8.50 am
Max Vento
Oxidative stress.

8.50 – 9.10 am
Hany Aly
Oxygen toxicity from mother to baby.

9.10 – 9.30 am
Neil Finer
SUPPORT trial report of oxygen arm.

9.30 – 9.50 am
Annie Janvier
Clinical ethics orientated resuscitation research.

9.50 – 10.10 am
MORNING TEA – Quarter Deck and Bridge

10.10 – 10.30 am (Chairperson: Keith Barrington)
Jennifer Dawson
SpO₂ and heart rate centiles in the delivery room – how should they be used?

10.30 – 10.50 am
Robert Kopotic
Comparison of cerebral and pulse oximetry.

10.50 – 11.10 am
Helmut Hummler
Brain tissue oxygenation during resuscitation.

11.10 – 11.30 am
Berndt Urllesberger
Regional oxygen saturation of the brain differs from peripheral tissue during transition of the newborn.

11.30 – 11.50 am
Richard Martin
Intermittent hypoxic episodes as an oxidant stress.

11.50 am – 12.10 pm
Wade Rich, Neil Finer or Max Vento
The PreSox trial.

12.10 pm
LUNCH – Dockside Restaurant
1.00 – 1.20 pm (Chairperson: Jeff Perlman)
Stuart Hooper
Facilitating lung aeration at birth.

1.20 – 1.40 pm
Claus Klingenberg
Devices for delivering sustained inflations.

1.40 – 2.00 pm
Edgardo Szyld
Study comparing a T piece vs a self inflating bag.

2.00 – 2.20 pm
Megan Wallace
Effect of a sustained inflation on markers of lung injury.

2.20 – 2.40 pm
Gianluca Lista
Sustained lung inflation in the delivery room: personal experience.

2.40 – 3.00 pm
Afternoon Tea – Quarter Deck and Bridge

3.00 – 3.20 pm (Chairperson: Peter Davis)
Tina Leone
End tidal CO₂ and ventilation in the delivery room.

3.20 – 3.40 pm
Georg Schmoelzer
Monitoring of respiratory function after birth: use of a Respiratory Function Monitor.

3.40 – 4.00 pm
John Kattwinkel
Effect of changing compliance on tidal volume delivery.

4.00 – 4.20 pm
Christoph Huenseler
Surfactant delivery through a thin catheter.

4.20 – 4.40 pm
Mario Rojas
Very early surfactant and nCPAP in the delivery room.

4.40 – 5.00 pm
Late Afternoon Tea – Quarter Deck and Bridge

5.00 – 5.20 pm
Neil Finer
The SUPPORT study – CPAP arm.

5.20 – 5.40 pm
Henrik Verder
Prediction (at birth) of RDS and which babies should receive surfactant.

5.40 – 6.00 pm
Thorsten Waloscheck
The Baby First initiative.

7.30 pm
Dinner – Dockside Restaurant

Thursday 6th May

8.00 – 8.20 am (Chairperson: Alan Jobe)
Graeme Polglaze
Effect of inflammation and ventilation on cerebral hemodynamics and injury.

8.20 – 8.40 am
Noah Hillman
Inflammatory progression after stretch injury of the fetal airway.

8.40 – 9.00 am
Suhas Kallapur
Modulation of inflammation – implications for resuscitation injury.

From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: May 12
Date: Friday, April 30, 2010 1:32:11 PM

Oh, yeah, sure.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 30, 2010 1:32 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: Re: May 12

I will write a script for my 5 minutes to introduce the study on the live teleconference for the press.

----- Original Message -----

From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Apr 30 13:30:45 2010
Subject: RE: May 12

I'm not following what you mean, but, I'm here and ready to help.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 30, 2010 12:21 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: May 12

Bob

If i write on on script to introduce the SUPPORT trial for the press for 5/12 can you assist with editing? This way, we can get nichd "out there."

Let me know and i can send you something

Rose

From: [Edward Donovan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: ****SUPPORT MASTEHEADS
Date: Thursday, April 29, 2010 10:43:35 PM

sounds good

Edward F. Donovan, M.D.
Ohio Perinatal Quality Collaborative
www.OPQC.net

Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0169
Fax 513-636-0171
www.cincinnatichildrens.org/cprc

From: Fanaroff, Avroy
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ****SUPPORT MASTEHEADS
Date: Thursday, April 29, 2010 3:27:00 PM

It's fine
Av

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, April 29, 2010 3:01 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; kristin zaterka
Subject: ****SUPPORT MASTEHEADS
Importance: High

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From: Hogan, Sharon [mailto:shogan@nejm.org]
Sent: Thursday, April 29, 2010 9:13 AM
To: 'Wally Carlo, M.D.'; Finer, Neil
Cc: Moskowitz, Deborah
Subject: RE: Your articles in the NEJM

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Volume 362:1477-1490 April 22, 2010 Number 16

Next ▶

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The NAVIGATOR Study Group

Please confirm that these changes would be okay.

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

Visit us at www.UHhospitals.org.

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"
Subject: FW: ****SUPPORT MASTEHEADS
Date: Thursday, April 29, 2010 3:02:00 PM
Importance: High

FYI

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 29, 2010 3:01 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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Program Scientist for the Neonatal Research Network

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Thursday, April 29, 2010 1:18 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Your articles in the NEJM

FYI

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center
402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

From: Hogan, Sharon [<mailto:shogan@nejm.org>]
Sent: Thursday, April 29, 2010 10:07 AM
To: Finer, Neil
Cc: Moskowitz, Deborah; Wally Carlo, M.D.
Subject: RE: Your articles in the NEJM

Bless you!

Thanks again,

Sharon

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Thursday, April 29, 2010 1:10 PM
To: Hogan, Sharon
Cc: Moskowitz, Deborah; Wally Carlo, M.D.
Subject: RE: Your articles in the NEJM

Hi Sharon .
I think this is a great idea!!
Many thanks for this suggestion
Neil Finer

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
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Sharon

Sharon Cloud Hogan
Manuscript Editor
The New England Journal of Medicine
10 Shattuck St.
Boston, MA 02115-6094
phone: 617-487-6564, 781-740-4482, or 1-800-445-8080
fax: 617-739-9864
shogan@nejm.org

From: Hogan, Sharon
Sent: Tuesday, April 27, 2010 3:47 PM
To: 'Wally Carlo, M.D.'; 'nfiner@ucsd.edu'
Cc: Moskowitz, Deborah
Subject: Your articles in the NEJM
Importance: High

Hi, Wally,

We need to make the affiliations lists and the appendixes in these two articles consistent, and we noticed that in your article the material is listed according to author order, whereas in Dr. Finer's article they are listed according to site (e.g., "all in North Carolina"). Please let us know which style we should use for both articles. Also, space is an issue for the first page of your article (and it may be for Dr. Finer's also), so we would like to move the affiliations into the Appendix.

I'm at 781-740-4482 today and tomorrow.

Thanks again,

Sharon Hogan

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Susan Hintz"
Subject: 3 3 05 DSMC Monitoring
Date: Monday, April 26, 2010 2:44:00 PM
Attachments: 3 3 05 DSMC Monitoring.doc

The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants

The SUPPORT Trial

DATA AND SAFETY MONITORING PLANS

Adverse Events

Data on the following potential adverse events that may be related to the study maneuver will be recorded and evaluated as part of continuous safety monitoring during the trial by RTI:

1. Air leak on admission to the NICU, or during the initial 14 days of life
2. The need for chest compressions, and/or epinephrine in the delivery room or NICU
3. The occurrence of severe IVH (Grades 3-4, Papile)
4. Death

As background information to help the DSMC monitor this trial, we are providing the following observational data from the network's generic database from January 1, 2002-December 31, 2004. The proportions listed give the overall rate of an adverse event in the network population for each of the gestational age subgroups. The range of proportions for each adverse event across centers is presented to provide an idea about the variation seen over the sites for these outcomes. It is hoped that this information will provide detailed background statistics regarding the population for study in this trial.

It is suggested by the SUPPORT Subcommittee that consideration for a recommendation to stop the trial based on a safety concern would need to involve a statistically significant difference in an adverse event between the treatment groups, and that the occurrence of the adverse event is outside of the limits of plausibility for that specific event according to the most recent Neonatal Research Network data presented below.

Table 1: Overall proportion, variability and ranges across network centers for infants with gestational age 24-27 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	3753	0.237	0.43	0.108-0.371
DR Chest compressions	4050	0.108	0.31	0.035-0.258
Pneumothorax	3861	0.087	0.29	0.023-0.195
Death within first 14 days	4055	0.159	0.37	0.092-0.325

Table 2: Overall proportion, variability and ranges across network centers for infants with gestational age 24-25 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	1599	0.327	0.47	0.153-0.520
DR Chest compressions	1805	0.133	0.34	0.029-0.340
Pneumothorax	1667	0.116	0.32	0.026-0.239
Death within first 14 days	1808	0.249	0.44	0.124-0.485

Table 3: Overall proportion, variability and ranges across network centers for infants with gestational age 26-27 weeks at birth

Variable	N	Proportion	SD	Range of proportion across centers
IVH grade (3 or 4)	2154	0.170	0.38	0.022-0.263
DR Chest compressions	2245	0.088	0.29	0.034-0.200
Pneumothorax	2194	0.066	0.25	0.022-0.155
Death within first 14 days	2247	0.086	0.28	0.039-0.160

Note: The sample includes infants that were born on or after Jan 1, 2002 that have reached status. SD denotes standard deviation.

Data Safety Monitoring Committee

The Data Safety Monitoring Committee will review the progress of the study with respect to efficacy and adverse events in a sequential fashion by using interim monitoring boundaries. O'Brien-Fleming¹ boundaries will be used for efficacy monitoring and will be constructed for four looks at the data at 25%, 50%, 75%, and 100% of outcome assessment. Pocock boundaries will be used for adverse event monitoring and will be viewed after every 30 infants have been enrolled. A special adverse event form will collect the information so that it may be entered into the data base in a timely fashion.

From: Hogan, Sharon
To: Higgins, Rosemary (NIH/NICHD) [E]; "Wally Carlo, M.D."; nfiner@ucsd.edu
Cc: Moskowitz, Deborah
Subject: RE: Your articles in the NEJM
Date: Tuesday, April 27, 2010 4:12:19 PM

Thanks. We will follow the style used in Dr. Finer's paper then, with the material organized according to site.

All best,

Sharon

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, April 27, 2010 4:10 PM
To: 'Wally Carlo, M.D.'; Hogan, Sharon; nfiner@ucsd.edu
Cc: Moskowitz, Deborah
Subject: RE: Your articles in the NEJM

"all in NC" etc can be deleted.

Both appendices should be similar (i.e. listed by sites) I am ok with whatever will work and acknowledges the appropriate people and institutions.

Rose

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Tuesday, April 27, 2010 3:07 PM
To: Hogan, Sharon; 'Wally Carlo, M.D.'; nfiner@ucsd.edu; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Moskowitz, Deborah
Subject: RE: Your articles in the NEJM

Rose.

What do you think we should do?

Wally

-----Original Message-----

From: Hogan, Sharon <shogan@nejm.org>
Sent: Tuesday, April 27, 2010 2:47 PM
To: 'Wally Carlo, M.D.' <WCarlo@peds.uab.edu>; 'nfiner@ucsd.edu' <nfiner@ucsd.edu>
Cc: Moskowitz, Deborah <dmoskowitz@nejm.org>
Subject: Your articles in the NEJM

Hi, Wally,

We need to make the affiliations lists and the appendixes in these two articles consistent, and we noticed that in your article the material is listed according to author order, whereas in Dr. Finer's article they are listed according to site (e.g., "all in North Carolina"). Please let us know which style we should use for both articles. Also, space is an issue for the first page of your article (and it may be for Dr. Finer's also), so we would like to move the affiliations into the Appendix.

I'm at 781-740-4482 today and tomorrow.

Thanks again,

Sharon Hogan

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

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From: Pearson, Gail (NIH/NHLBI) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; Pemberton, Victoria (NIH/NHLBI) [E]
Subject: RE: PAS clinical research networks topic symposium
Date: Tuesday, April 27, 2010 12:17:20 PM

Sounds perfectly reasonable, Rose, thanks for letting us know!

Bset,

Gail

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, April 27, 2010 12:17 PM
To: Pearson, Gail (NIH/NHLBI) [E]; Pemberton, Victoria (NIH/NHLBI) [E]
Subject: PAS clinical research networks topic symposium

Gail and Victoria,

ON Sunday, May 2, one of our clinical trials (SUPPORT) is being presented at 4:15 PM so I will leave the session and return so that I can hear our trial presented.

Let me know if you think this will be a problem.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Preterm Studies Script
Date: Monday, April 26, 2010 3:53:31 PM

OK. You've seen this before; I just wanted you to have the most recent version, in case you get questions from the NHLBI program staff.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Monday, April 26, 2010 3:53 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Preterm Studies Script

I am looking at the press release now
Rose

From: Bock, Robert (NIH/NICHD) [E]
Sent: Monday, April 26, 2010 3:52 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Preterm Studies Script

Looks good. I'll accept them, print it out on an 11 by 7 and bring it for you tomorrow.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Monday, April 26, 2010 3:48 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: Preterm Studies Script

My changes
Rose

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: ["Susan Hintz"](#)
Subject: [Carlo, SUPPORT Oxygen Saturations, 2010-04-13.ppt](#)
Date: Monday, April 26, 2010 2:36:00 PM
Attachments: [Finer, SUPPORT CPAP, 2010-04-23 with NHLBI logo.ppt](#)
[Carlo, SUPPORT Oxygen Saturations, 2010-04-13.ppt](#)



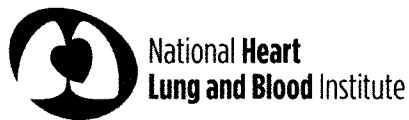
Randomized Trial of Early CPAP versus Surfactant in Extremely Preterm Infants



The SUPPORT Trial



The SUPPORT Study Group of the
Eunice Kennedy Shriver NICHD
Neonatal Research Network



Disclosure Statement

Dr. Finer has documented that he has no relevant financial relationships to disclose or COIs to resolve

Dr. Finer has documented that his presentation will not involve discussion of unapproved or off-label, experimental or investigational use agents.

Background

- ✓ Surfactant treatment at less than 2 hours of life significantly decreases death, air leak, and death or bronchopulmonary dysplasia (BPD) in preterm infants- but not BPD alone.
- ✓ However, no surfactant studies had a comparison group who received early CPAP
- ✓ Several studies have demonstrated that the use of surfactant does not significantly affect the risk of subsequent neurodevelopmental impairment



Background



- ✓ Retrospective cohort studies demonstrated that the early use of CPAP in very preterm infants with respiratory distress may decrease mechanical ventilation without increased morbidity and without surfactant.
- ✓ Morley et al reported in the COIN Trial of 610 infants between 25 0/7 to 28 6/7 weeks gestation, who were able to breathe at 5 minutes of age and had evidence of respiratory distress.

COIN Trial

Morley et al. NEJM2008; 358(7):700-708

- ✓ Randomized to intubation and ventilation, OR CPAP at 8 cm H₂O; CPAP infants were intubated if they met failure criteria.
- ✓ No requirement for surfactant administration
- ✓ CPAP group had:
 - no significant reduction in death or oxygen at 36 weeks (the primary outcome),
 - significantly higher pneumothoraces (9.1% vs. 3.0%), most within the first 2 days

Hypothesis

We hypothesized that early CPAP with a limited ventilator strategy would reduce the incidence of death or survival with BPD at 36 weeks compared to early Surfactant

Method – Patients

- ✓ Inborn infants of 24^{0/7} to 27^{6/7} weeks gestation for whom a decision had been made to provide full resuscitation were eligible
- ✓ Antenatal Parental consent was obtained
- ✓ Enrollment from February 2005 to February 2009
- ✓ Randomization was stratified by center and by gestational age (24 and 25 weeks; 26 and 27 weeks)

Factorial Design

- ✓ Infants also randomized to 2 ranges of SpO₂ using purpose built blinded oximeters
- ✓ Results of this Trial presented by Dr Carlo at Clinical Epidemiology Session

CPAP Intervention

- ✓ In the delivery room, CPAP at 5 cm H₂O was provided until NICU admission using a T-piece resuscitator, a neonatal ventilator, or an equivalent methodology
- ✓ Intubation only for infants who required intubation for resuscitation based on standard NRP indications, not performed for the surfactant administration
- ✓ Intubated infants given surfactant

Methods:

	CPAP Arm	Surfactant
Delivery Room	<ul style="list-style-type: none">• 5 cm H₂O• Intubation per NRP• If intubated, surfactant	<ul style="list-style-type: none">• Standard NRP
Intubation/ Surfactant	<ul style="list-style-type: none">• Considered if:• FiO₂ > 0.5• PaCO₂ > 65• Hemodynamic instability	<ul style="list-style-type: none">• Prior to 1 hour

Methods: Extubation Criteria

Within 24 hrs of meeting all criteria

CPAP/Limited Ventilation	Surfactant
<ul style="list-style-type: none">•FiO₂ < 0.50 and MAP < 10 cm•PaCO₂ < 65••	<ul style="list-style-type: none">•FiO₂ < 0.35 and MAP ≤ 8 cm•PaCO₂ < 50••

Methods – Duration of Intervention

- ✓ The criteria for both arms were in effect for the first 14 days of life, following which the infant was treated as per NICU standard practice.
- ✓ For both arms, intubation could be performed at any time for the occurrence of repetitive apnea requiring bag and mask ventilation, clinical shock, sepsis, and/or the need for surgery.

Methods – BPD Definitions

- ✓ For the primary outcome, BPD was defined using the physiologic definition:
 - ✓ receipt > 30% oxygen at 36 weeks
 - ✓ need for positive pressure support
 - ✓ If $FiO_2 < .30$, oxygen withdrawal performed
- ✓ Pre-specified secondary outcomes included the evaluation of BPD defined by the receipt of oxygen at 36 weeks.

Results – Patient Population

	CPAP (N = 663)	Surfactant (N = 653)
Birthweight*	835 ± 188.2	826 ± 198.1
Gestational Age*	26.2 ± 1.1	26.2 ± 1.1
24 to 25 6/7ths (%)	43	43
26 to 27 6/7ths (%)	57	57
Race, White/Black/Hispanic (%)	38 / 38 / 21	36 / 42 / 19
Antenatal corticosteroids (%)	97	96
Multiple births (%)	27	24

*Mean ± Standard Deviation

Results – Primary Outcome

	CPAP N=663	Surfactant N=653	Adjusted Relative Risk (95% CI)
Death or BPD (Physiologic)	47.8%	51.0%	0.95 (0.85, 1.05)
BPD - Physiologic	39.2%	40.6%	0.99 (0.87, 1.14)
Death by 36 weeks PMA	14.2%	17.5%	0.81 (0.63, 1.03)

Results – Delivery Room

Variable	CPAP (N=663)	Surfactant (N=653)	Relative Risk for CPAP vs. Surfactant (95% CI)	Adjusted P- value
Apgar at 1 minute <3	23.3%	25.6%	0.92 (0.76, 1.11)	0.38
Apgar at 5 minutes <3	3.9%	4.9%	0.82 (0.5, 1.34)	0.43
PPV in the DR	65.7%	92.9%	0.71 (0.67, 0.75)	<0.0001
Intubated in DR	34.4%	93.4%	0.37 (0.34, 0.42)	<0.0001
DR intubation for resuscitation	32.6%	27.0%	1.21 (1.02, 1.43)	0.02
Surfactant DR/NICU	67.1%	98.9%	0.67 (0.64, 0.71)	<0.0001
Epinephrine in DR	2.0%	4.1%	0.48 (0.25, 0.91)	0.02

Results – Other Pre-specified Outcomes

	CPAP N=663	Surfactant N=653	Relative Risk or Difference in Means
BPD (O ₂ use at 36 wks)	40.2%	44.3%	0.94 (0.82, 1.06)
Death/BPD, 36 wks	48.7%	54.1%	0.91 (0.83, 1.01)
Severe ROP- survivors	13.1%	13.7%	0.94 (0.69, 1.28)
Any air leaks (14 days)	6.8%	7.4%	0.89 (0.6, 1.32)
Mechanical Vent Survivors (Days)	24.8 ± 1.0	27.7 ± 1.1	-3.0 (-5.6, -0.3)*
Alive and off MV at 7 days	55.3%	48.8%	1.14 (1.03, 1.25)*
Postnatal steroids for BPD	7.2%	13.2%	0.57 (0.41, 0.78)*

* = p<0.05

SUPPORT – Other Results

No differences in the incidence of:

- ✓ PDA, PDA requiring surgery,
 - ✓ NEC, medical or surgical
 - ✓ Severe IVH/PVL
-
- ✓ In the 24 to 25 weeks strata CPAP infants had a lower mortality than Surfactant infants:
 - CPAP 23.9% vs Surfactant 32.1%
 - Relative Risk difference 0.74 (0.57, 0.98)

SUMMARY

- ✓ No significant difference for primary outcome of death or BPD
- ✓ More CPAP infants were alive and off mechanical ventilation by day 7 ($p=0.011$)
- ✓ CPAP infants received less postnatal steroids for BPD ($p<0.001$) and required fewer vent days ($p=0.03$).
- ✓ CPAP Infants 24 to 25 6/7 weeks had a significantly lower mortality rate while hospitalized ($p<.01$)
- ✓ CPAP infants did not have increased morbidities

Conclusions

- ✓ Early CPAP with a limited ventilator strategy for the extremely low birth weight infant is associated with decreased exposure to intubation and mechanical ventilation, decreased death in the most immature infants, without any increase in measured morbidities
- ✓ All surviving infants will be followed to 18-22 months for a complete neurodevelopmental assessment

**Thanks to the many parents, infants,
and NICU staff**

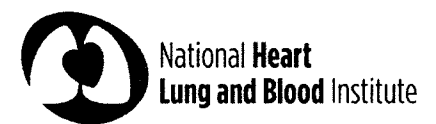


**Special Thanks to the Research
Coordinators of the NRN**

Study Funded by the NICHD and NHLBI

NICHD Neonatal Research Network Centers (2005-2009)

- Brown University
- Case Western Reserve Univ
- Duke University
- Emory University
- Indiana University
- RTI International
- Stanford University
- Tufts Medical Center
- University of Alabama – Birmingham
- University of California – San Diego
- University of Cincinnati
- University of Iowa
- University of Miami
- University of New Mexico
- University of Rochester
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- University of Utah
- Wake Forest University
- Wayne State University
- Yale University



3546 Infants were assessed for eligibility (3127 pregnancies)*

235 Did not meet eligibility criteria
125 Personnel/Equipment not available
699 Eligible but consent not sought
344 Parent unavailable for consent
748 Consent denied by parent or guardian
11 Excluded for other reasons
68 Consented but not randomized

1316 Underwent randomization

663 Were assigned CPAP

653 Were assigned Surfactant

94 Died before discharge

569 Survived to discharge, transfer one year of life

114 Died before discharge

539 Survived to discharge, transfer or one year of life

223 BPD Physiologic

346 No BPD Physiologic

219 BPD Physiologic

320 No BPD Physiologic

Consort Diagram

3546 Infants were assessed for eligibility (3127 pregnancies)

235 Did not meet eligibility criteria
125 Personnel/Equipment not available
699 Eligible but consent not sought
344 Parent or guardian unavailable
748 Consent denied by parent or guardian
11 Excluded for other reasons
68 Consented but not randomized

1316 Underwent randomization

654 Randomized to oxygen saturation targeting 85-89%

662 Randomized to oxygen saturation targeting 91-95%

336 Randomized to early CPAP

318 Randomized to early surfactant

327 Randomized to early CPAP

335 Randomized to early surfactant

54 Died 282 Survived

60 Died 258 Survived

40 Died 287 Survived

54 Died 281 Survived

103 BPD 179 No BPD

102 BPD 156 No BPD

120 BPD 167 No BPD

117 BPD 164 No BPD

Methods – Sample Size Estimate

- Baseline rate of BPD/Death of 50%
- Absolute risk difference of 10%
- Increased by 1.12 to allow for multiples randomized to same treatment
- Increased by 1.17 to adjust for attrition
- Increased further to minimize Type I error using a conservative 2% level of significance
- Final sample size was 1310 infants

Methods – Data Analysis

- The primary and categorical outcomes were analyzed using Poisson regression implementation in a Generalized Estimating Equation (GEE) model to obtain adjusted relative risk and 95% CI
- Continuous outcomes were analyzed using mixed effects linear models to produce adjusted means and standard errors
- Adjustment was performed for pre-specified stratification (center and GA) and for familial clustering as multiple births were randomized to the same treatment arms

Pre-Specified Outcomes for 24 to 25 week Stratum

Characteristic	CPAP (N=285)	Surfactant (N=280)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	63.9% (182/285)	67.9% (190/280)	0.96 (0.85, 1.07)	0.45
BPD (supplemental oxygen) or death by 36 weeks PMA	62.8% (179/285)	67.1% (188/280)	0.95 (0.84, 1.06)	0.36
BPD (physiologic definition) by 36 weeks PMA	54.8% (125/228)	54.5% (108/198)	1.06 (0.91, 1.25)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	53.5% (122/228)	53.5% (106/198)	1.05 (0.9, 1.23)	0.53
Death by 36 weeks PMA	20.0% (57/285)	29.3% (82/280)	0.68 (0.5, 0.92)	0.01
Days on supplemental oxygen† Adjusted Mean±StdErr,	80.8 ± 2.3	80.3 ± 2.4	0.5 (-5.8, 6.9)	0.86
Unadjusted Median (IQR) (N=421)	79.5 (51.5, 108.5)	79 (52, 110)		
Days on mechanical vent (HFV & CV) † Adjusted	35.8 ± 1.5	38.7 ± 1.6	-3.0 (-7.2, 1.3)	0.17
Mean±StdErr, Unadjusted Median (IQR) (N=421)	29.5 (10, 48)	33 (14, 56)		
Alive and off MV (HFV/CV) at 7 days	34.3% (97/283)	26.4% (74/280)	1.29 (1, 1.66)	0.049
Any air leak in first 14 days	8.1% (23/285)	9.6% (27/280)	0.79 (0.47, 1.35)	0.40
Medical or surgical NEC	15.1% (42/279)	13.1% (35/268)	1.13 (0.74, 1.71)	0.58
IVH grade 3-4	19.8% (54/273)	17.0% (45/265)	1.17 (0.82, 1.68)	0.39
Postnatal steroids for BPD	13.0% (36/276)	20.5% (54/264)	0.66 (0.46, 0.94)	0.02

Pre-Specified Outcomes for 26 to 27 week Stratum

Characteristic	CPAP (N=378)	Surfactant (N=373)	Relative Risk or Difference in Means for CPAP vs. Surfactant (95% CI)	Adjusted P- value
BPD (physiologic definition) or death by 36 weeks PMA	35.7% (135/378)	38.3% (143/373)	0.94 (0.78, 1.13)	0.48
BPD (supplemental oxygen) or death by 36 weeks PMA	38.1% (144/378)	44.2% (165/373)	0.87 (0.74, 1.03)	0.12
BPD (physiologic definition) by 36 weeks PMA	28.7% (98/341)	32.6% (111/341)	0.92 (0.74, 1.15)	0.46
BPD (supplemental oxygen) by 36 weeks PMA	31.4% (107/341)	39.0% (133/341)	0.84 (0.69, 1.02)	0.08
Death by 36 weeks PMA	9.8% (37/378)	8.6% (32/373)	1.12 (0.72, 1.75)	0.61
Days on mechanical vent (HFV & CV) † Adjusted Mean±StdErr, Unadjusted Median (IQR) (N=677)	13.7 ± 1.3 4 (0, 15)	16.7 ± 1.3 6 (2, 21)	-3.0 (-6.4, 0.4)	0.08
Alive and off MV (HFV/CV) at 7 days	71.2% (265/372)	65.6% (244/372)	1.09 (0.98, 1.2)	0.10
Any air leak in first 14 days	5.8% (22/378)	5.6% (21/373)	1.01 (0.57, 1.81)	0.97
Medical or surgical NEC	10.9% (41/375)	7.6% (28/368)	1.42 (0.9, 2.25)	0.14
IVH grade 3-4	10.3% (38/369)	7.4% (27/363)	1.41 (0.86, 2.3)	0.17
Postnatal steroids for BPD	2.9% (11/373)	7.9% (29/367)	0.4 (0.2, 0.78)	0.008

Comparison with Previous Studies

COIN Trial – NEJM 2008;358:700-8

- Infants of 25 to 28wks, Breathing @ 5 minutes
- 610 infants vs 1316 infants
- No protocol for surfactant, 8 cm H₂O
- Infants 26.9 wks vs 26.2 wks, 960 vs 830gm
- Death /BPD @ 36 wks – 33.9 vs 38.9 – 48.7 vs 54.1
- Air leaks – 9% vs 3% - higher in CPAP
- SUPPORT - 6.8% vs 7.4%

Comparison with Previous Studies

Rojas et al – Pediatrics 2009;123:137-42

- 279 infants from 27 to 31 wks
- Compared CPAP to intubation/surfactant and extubation within 1 hr of birth
- Excluded 5 min Apgar < 2, intubated within 15 min, PROM > 3 wks
- Air leaks higher in CPAP – 9% vs 2%
- Early Intub/Surf had lesser BPD 49% vs 59% but only significant for 30-31 wk infants



Randomized Trial of Oxygen Saturation Targets in Premature Infants - the SUPPORT Trial

The SUPPORT Study Group of the
Eunice Kennedy Shriver NICHD
Neonatal Research Network



Disclosure Statement

Dr. Carlo has documented that he has no relevant financial relationships to disclose or COIs to resolve

Background

- Retinopathy of prematurity (ROP) continues to be an important cause of blindness in preterm infants
- Recent observational data suggest that oxygen saturations in the lower limits of common clinical practice (83 or 85%) may reduce ROP but this has not been tested in RCTs
- Furthermore, in RCTs of oxygen supplementation to reduce ROP conducted in the 1950s, restriction of oxygen supplementation resulted in an increased mortality in infants in the lower oxygen group

Hypothesis

A lower O₂ saturation target range (85 to 89%)
compared to
a higher O₂ saturation target range (91 to 95%)
reduces
the incidence of the composite outcome of
severe ROP or death
among
infants of 24^{0/7} to 27^{6/7} weeks gestational age

Method – Patients

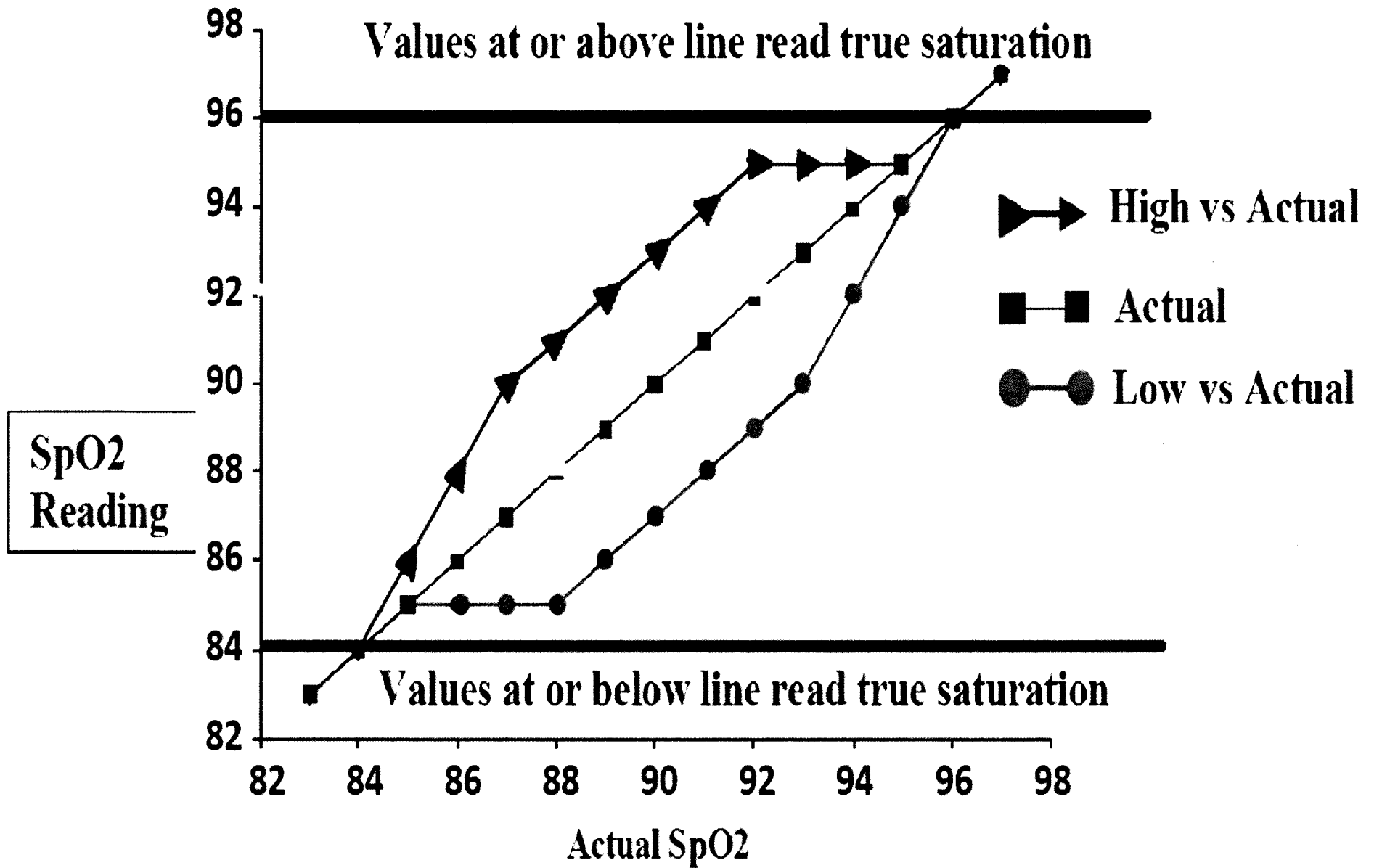
- Inborn infants of 24^{0/7} to 27^{6/7} weeks gestation for whom a decision had been made to provide full resuscitation were eligible
- Parental consent was obtained antenatally
- Enrollment from February 2005 to February 2009
- Randomization was stratified by center and by gestational age:
 - 24 and 25 weeks
 - 26 and 27 weeks

Methods – Intervention (1)

- Infants were randomized to:
 - lower saturation targeting (85 to 89%) or;
 - higher saturation targeting (91 to 95%)
- Oxygen saturations were monitored with electronically-altered Masimo Radical Pulse Oximeter

SpO ₂ Group	Displayed Target	Actual Target	Alarm Values
Low SpO ₂	88-92%	85-89%	<85 and >95%
High SpO ₂	88-92%	91-95%	<85 and >95%

Actual vs Low and Hi Reading SaO2



Methods – Intervention (2)

- Oxygen saturation targeting was initiated within the first two hours after birth and was continued until 36 weeks post-menstrual age or until the infant remained on room air and off the ventilator/CPAP for >72 hours, whichever occurred first
- Adjustments in supplemental oxygen to maintain the displayed saturation within the target range of 88 to 92% were performed by the clinical staff, not the researchers

Methods – Factorial Design

- Infants were also randomized to CPAP started at birth or intubation with surfactant
- Results of the CPAP/surfactant Trial were presented by Dr. Finer at the Clinical Trials session

Methods – ROP Assessments

- Trained ophthalmologists followed the infants until the study endpoint *or* fully vascularized retinas *or* immature vessels in zone III for two consecutive exams in each eye were documented
- Severe retinopathy was defined as threshold retinopathy if any of the following were present:
 - In zone I: stage 3 ROP; plus disease with any stage of ROP
 - In zone II: plus disease with stage 2 or 3 ROP
 - If ophthalmologic surgery and/or bevacizumab ROP treatment was used

Methods – Sample Size Monitoring and Analysis

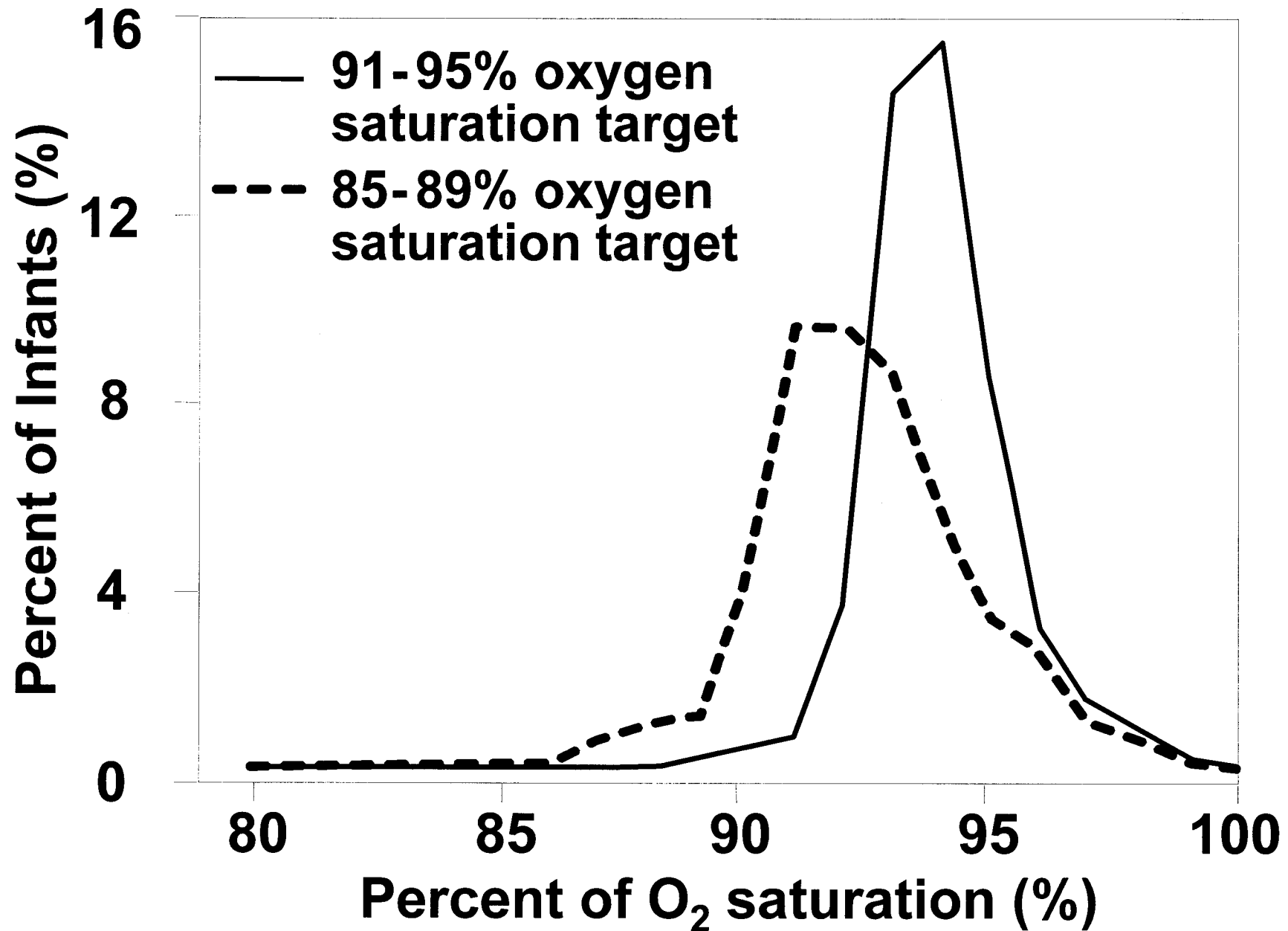
- Based on an absolute difference of 10% in the primary outcome, sample size was 1310
- An independent DSMC reviewed primary outcomes and adverse events at 25%, 50%, and 75% of outcome assessment
- The DSMC evaluated compliance with oxygen saturation targeting
- Adjustment was performed for pre-specified stratification (center and GA) and for familial clustering as multiple births were randomized to the same treatment arms

Results – Patient Population*

	Lower Saturation Group (N = 654)	Higher Saturation Group (N = 662)
Birth weight	836±193 grams	825±193 grams
Gestational age	26±1 weeks	26±1 weeks
Race, White/Black/Hispanic	37/39/20%	42/35/19%
Antenatal corticosteroids	96.8%	95.6%
Multiple births	24.6%	26.6%

*All p values >0.05

Actual Median Oxygen Saturation (%)



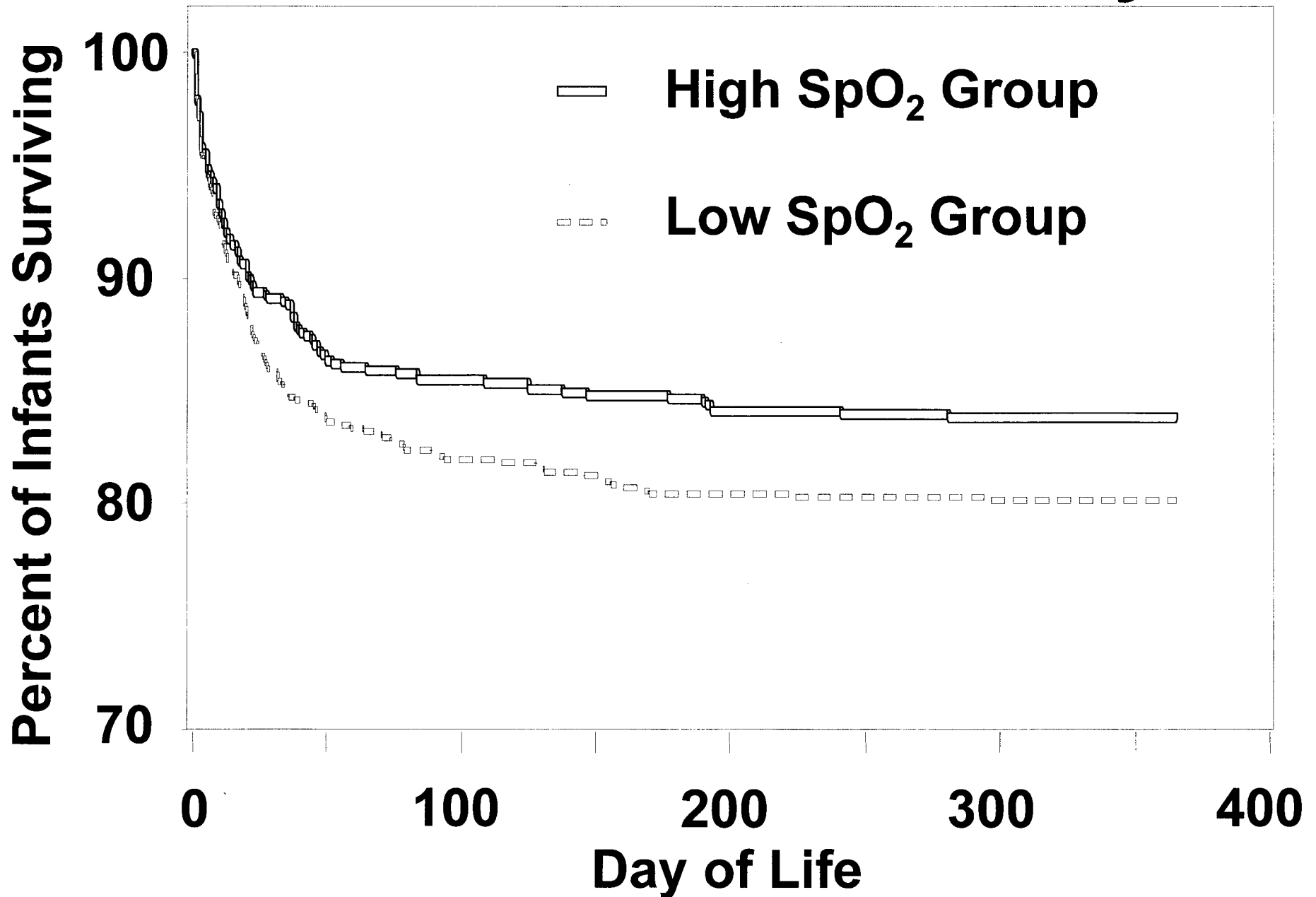
Results – Primary Outcome

	Lower Saturation Group N=654	Higher Saturation Group N=662	Adjusted Relative Risk (95% CI)	
Severe ROP/death	28.3%	32.1%	0.90 (0.76, 1.06)	
Severe ROP	8.6%	17.9%	0.52 (0.37, 0.73)	NNT=11
Death	19.9%	16.2%	1.27 (1.01, 1.60)	NNH=27

Results – ROP Adjudication Analysis

	Lower Saturation Group N=654	Higher Saturation Group N=662	Relative Risk for Low SpO ₂ vs. High SpO ₂ (95% CI)	
Severe ROP	8.6%	17.9%	0.52 (0.37, 0.73)	NNT=11
Severe ROP with adjudication (98.6%)	8.0%	16.6%	0.52 (0.37, 0.73)	NNT=12
Severe ROP with ROP if lost to F/U (100%)	10.1%	17.5%	0.62 (0.45, 0.84)	NNT=14

Survival Curve for Mortality



Results – BPD and other pulmonary outcomes

	Lower Saturation Group N=654	Higher Saturation Group N=662	Adjusted Relative Risk (95% CI)
BPD (O ₂ use at 36 w)	37.6%	46.7%	0.82 (0.72, 0.93)
BPD (O ₂ use) or death, 36 w	48.5%	54.2%	0.91 (0.83, 1.01)
BPD (phys), 36 w	38.0%	41.7%	0.92 (0.81, 1.05)
BPD (phys) or death, 36 w	48.8%	50.0%	0.99 (0.90, 1.10)
Pneumothorax	7.2%	6.5%	1.12 (0.74, 1.68)
Any air leaks (14 days)	7.8%	6.3%	1.23 (0.83, 1.83)
Postnatal steroids for BPD	9.6%	10.7%	0.91 (0.67, 1.24)

Results – PDA

	Lower Saturation Group N=654	Higher Saturation Group N=662	Adjusted Relative Risk (95% CI)
PDA	47.9%	50.0%	0.96 (0.86, 1.07)
Medical R _x for PDA	34.5%	36.1%	0.95 (0.82, 1.09)
Surgical R _x for PDA	11.4%	10.5%	1.09 (0.80, 1.48)

Results – Other Major Outcomes

	Lower Saturation Group N=654	Higher Saturation Group N=662	Adjusted Relative Risk (95% CI)
IVH, grade 3 or 4	13.2%	12.7%	1.06 (0.80, 1.40)
PVL	3.8%	4.7%	0.83 (0.49, 1.42)
NEC, stage ≥ 2	11.9%	10.8%	1.11 (0.82, 1.51)
Late onset sepsis	36.5%	35.6%	1.03 (0.89, 1.18)

Summary

- O₂ saturation targeting in the range of 85-89% did not affect severe ROP/death
- O₂ saturation targeting in the range of 85-89% resulted in a significant reduction in severe ROP (17.9 to 8.6%, NNT = 11)
- However, mortality was significantly increased in the 85-89% target group (19.9 versus 16.2%, NNH = 27)

Conclusions

- Lower oxygen saturation targeting, as conducted in this trial, did not reduce severe ROP/death
- Lower oxygen saturation targeting, as conducted in this trial, decreased severe ROP
- The potential to reduce the risk of severe ROP must be carefully weighed against the possibility of increased risk of death
- Follow up of these infants and data from the similarly designed ongoing trials will be important

**Thanks to the many parents,
infants, and NICU staff**



**Thanks to the members of the
Neonatal Research Network**

NICHD Neonatal Research Network Centers (2005-2009)

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- RTI International
- Stanford University
- Tufts Medical Center
- University of Alabama – Birmingham
- University of California – San Diego
- University of Cincinnati
- University of Iowa
- University of Miami
- University of New Mexico
- University of Rochester
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- University of Utah
- Wake Forest University
- Wayne State University
- Yale University



Results – Causes of Death

	Lower Saturation Group (N = 130)	Higher Saturation Group (N = 107)
Respiratory distress syndrome	23.8%	29.0%
Infection	19.2%	19.6%
Necrotizing enterocolitis	17.7%	13.1%
Bronchopulmonary dysplasia	10.8%	9.3%
Central nervous system insult	9.2%	8.4%
Immaturity	5.4%	2.8%
Other	13.8%	17.8%

Other Outcomes

	Lower Saturation Group	Higher Saturation Group	Adjusted p value
Length of stay (days) m+SE	104 ± 2.0	106 ± 2.0	0.45
Duration of MV (days) m+SE	26 ± 1	27 ± 1	0.30
Duration of O ₂ suppl (days) m+SE	60 ± 2	67 ± 2	0.0002
CPAP (days) m+SE	17 ± 1	17 ± 1	0.94
Nasal SIMV (days) m+SE	3 ± 0.3	4 ± 0.3	0.14

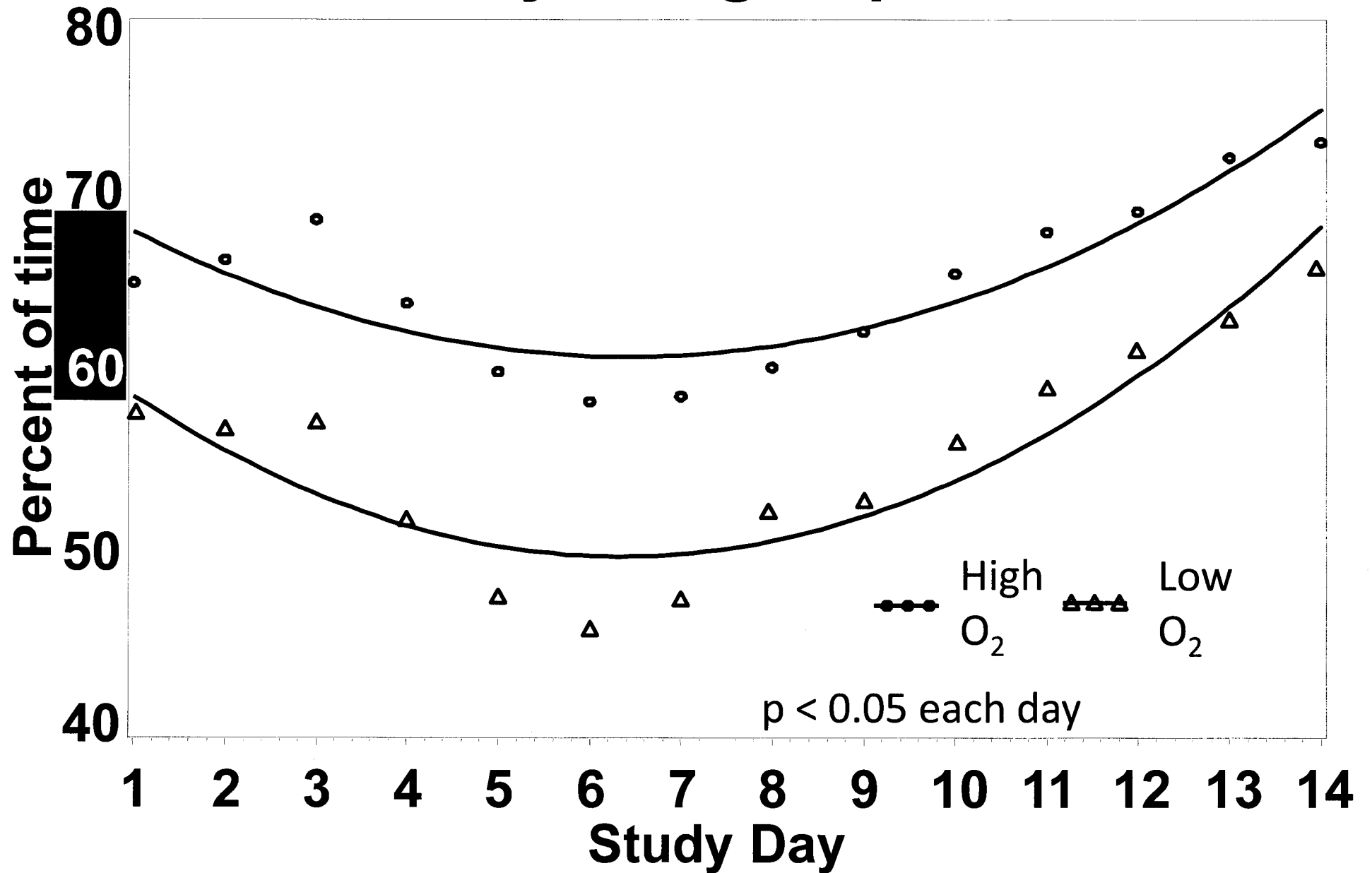
Mean percent of time spent in SpO₂ ranges while on supplemental oxygen

SpO ₂ range	Lower Saturation Group Mean % of time in range (95% CI)	Higher Saturation Group Mean % of time in range (95% CI)	p value
>96%	20.1 (18.8, 21.3)	23.2 (22.0, 24.5)	0.0001
<80%	7.3 (6.6, 8.1)	5.5 (4.8, 6.3)	0.0002
<75%	4.5 (3.8, 5.2)	3.6 (2.9, 4.3)	0.0486
<70%	2.5 (1.9, 3.1)	2.1 (1.5, 2.7)	0.4090

Median percent of time spent in SpO₂ ranges while on supplemental oxygen

SpO ₂ range	Lower Saturation Group Median % of time in range	Higher Saturation Group Median % of time in range	p value
>96%	16.0	19.6	<0.0001
<80%	5.9	3.9	<0.0001
<75%	3.3	2.1	<0.0001
<70%	1.5	0.9	<0.0001

Percent of time on oxygen by day and group



3546 Infants were assessed for eligibility (3127 pregnancies)*

235 Did not meet eligibility criteria
125 Personnel/Equipment not available
699 Eligible but consent not sought
•Parent unavailable for consent
•Consent denied by parent or guardian
11 Excluded for other reasons
68 Consented but not randomized

1316 Underwent randomization

654 Were assigned to oxygen saturation targeting 85-89%

662 Were assigned to oxygen saturation targeting 91-95%

130 Died before discharge

524 Survived to discharge, transfer one year of life

107 Died before discharge

555 Survived to discharge, transfer or one year of life

41 Severe ROP

434 No severe ROP

49 Final ROP outcome missing

91 Severe ROP

418 No severe ROP

46 Final ROP outcome missing

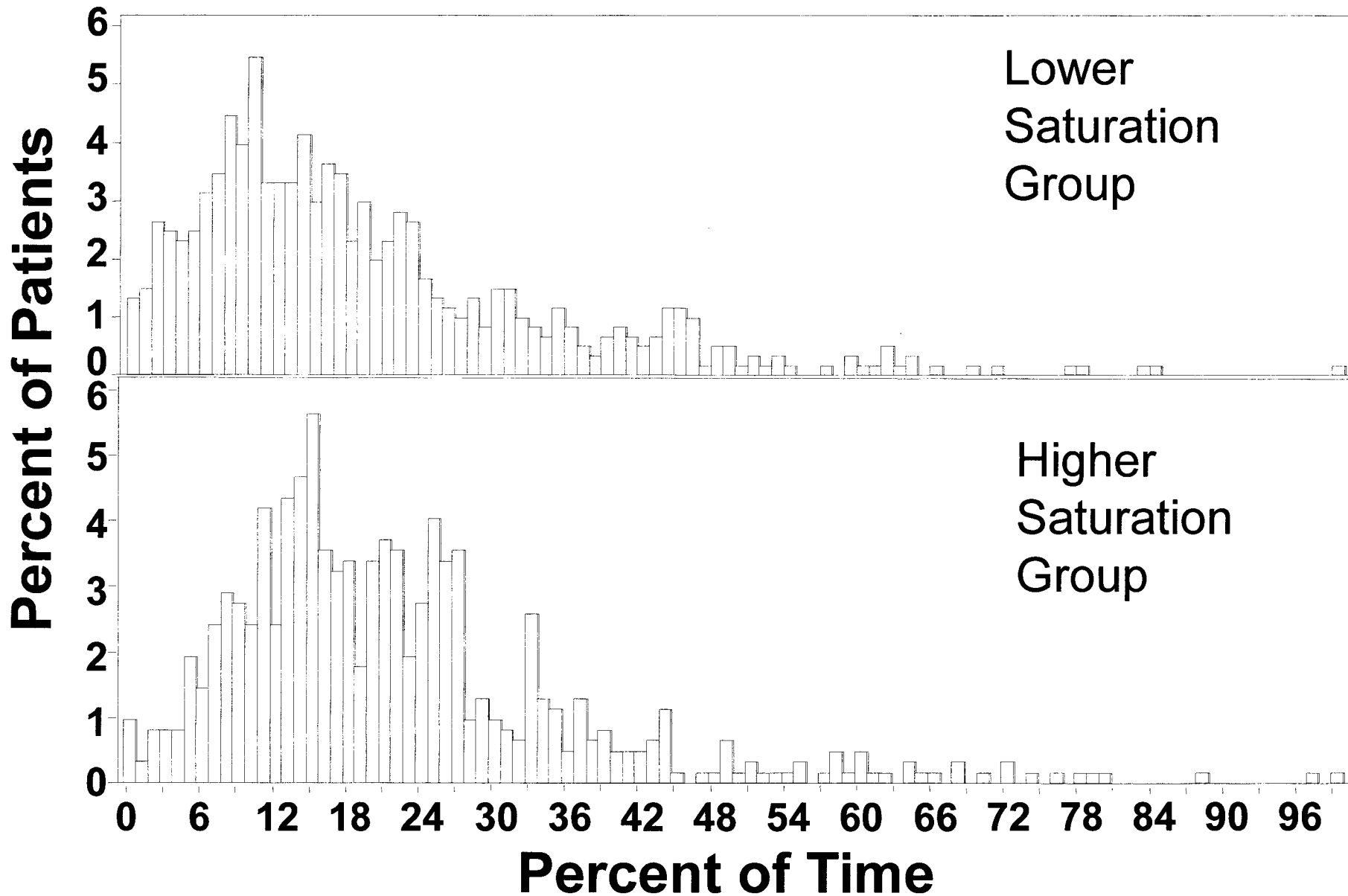
Methods – Data Analysis

- The primary and categorical outcomes were analyzed using Poisson regression implemented in a Generalized Estimating Equation (GEE) model to obtain adjusted relative risk and 95% CI
- Continuous outcomes were analyzed using mixed effects linear models to produce adjusted means and standard errors
- Adjustment was performed for pre-specified stratification (center and GA) and for familial clustering as multiple births were randomized to the same treatment arms

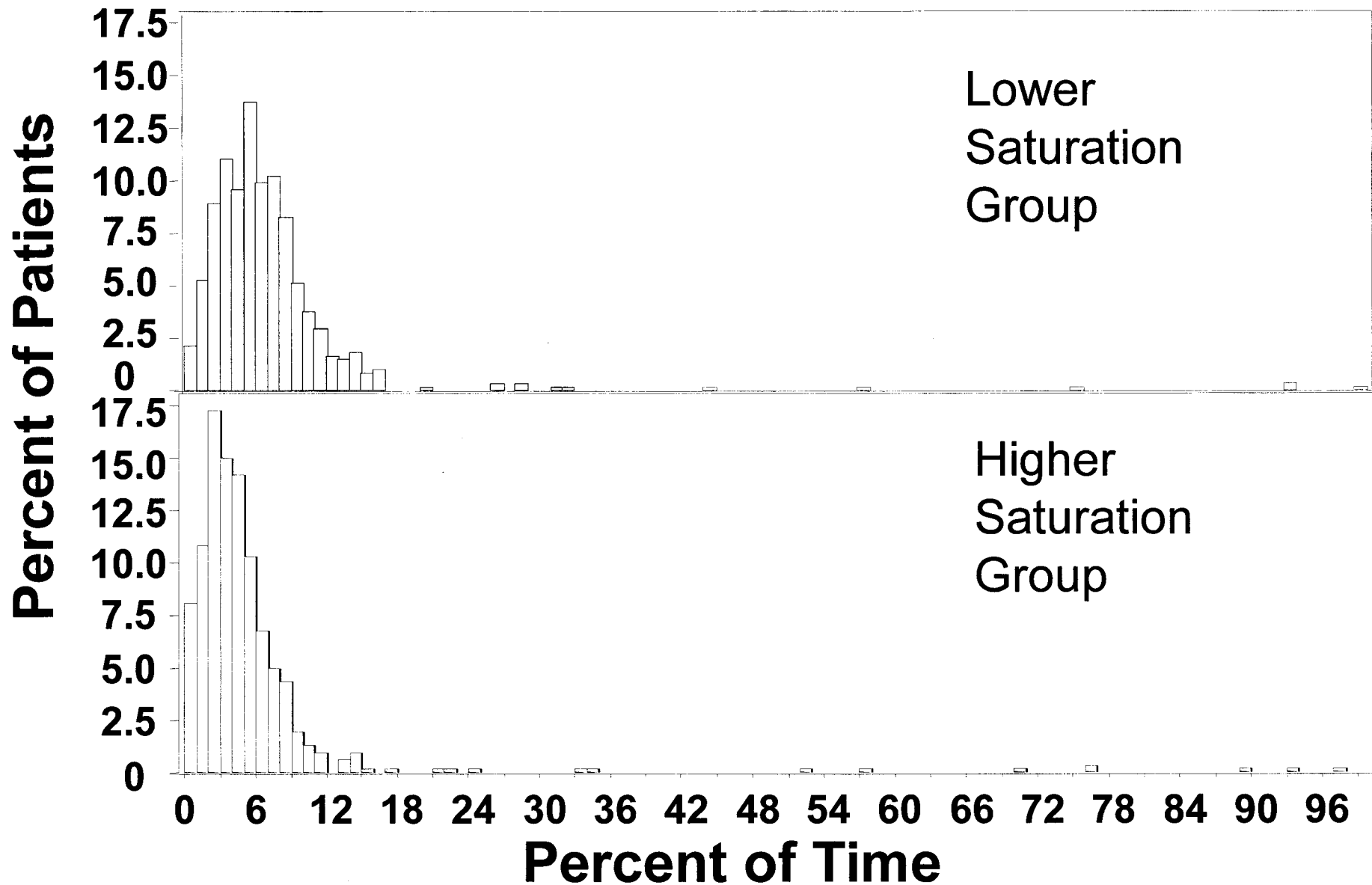
Methods – Sample Size Estimate

- Baseline rate of severe ROP/Death of 50%
- Absolute risk difference of 10%
- Increased by 1.12 to allow for multiples randomized to same treatment
- Increased by 1.17 to adjust for attrition
- Increased further to minimize Type I error using a conservative 2% level of significance
- Final sample size was 1310 infants

Percent of time with SpO₂ values >96% while on supplemental oxygen



Percent of time with SpO₂ values <80% while on supplemental oxygen



From: [Wally Carlo, M.D.](#)
To: [Monica Collins](#)
Cc: [Hastings Betty J.](#); [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: Following the Support Study
Date: Tuesday, April 26, 2005 10:55:21 AM

Monica: Let me discuss this on the SUPPORT conf call. Wally

From: Monica Collins
Sent: Tuesday, April 26, 2005 9:25 AM
To: Wally Carlo, M.D.
Subject: Following the Support Study

Wally,

Betty and I spoke about RTI providing some type of analysis of compliance for the Support Trial with rapid feedback to the center. We thought something similar to what was done in the SAVE trial. She asked if you can be very specific and come up with a plan to provide what information, to who (center or sub-committee), etc.

She says it should be easy, but it will be no more frequent than the downloads which are scheduled for 30 days and transmission is only once per week.

Monica

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Friday, April 23, 2010 11:51 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: RE: logo
Attachments: SUPPORT Final rev PAS-ATS April 23.ppt

Done
Looks good – their new logo!!

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center
402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, April 23, 2010 8:39 AM
To: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: FW: logo

NHLBI has an updated logo – can you apply this one to the slides??
Thanks
Rose

From: Nguyen, Cuong (NIH/NHLBI) [E]
Sent: Friday, April 23, 2010 11:37 AM
To: Blaisdell, Carol (NIH/NHLBI) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: logo

Dear All,

Logo is attached.

Cuong

From: Blaisdell, Carol (NIH/NHLBI) [E]
Sent: Friday, April 23, 2010 11:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Nguyen, Cuong (NIH/NHLBI) [E]
Subject: RE: logo

Rose,
For your presentation at Pediatric Academic Society meeting next week,

Here is a template slide with our logo, not sure you can pick up the logo and move it though.
Cuong who works with our lung division director may have other ideas.

cb

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 10:27 AM
To: Blaisdell, Carol (NIH/NHLBI) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: logo

Carol

Do you have an NHLBI logo that we could insert onto a POWERPOINT slide for the upcoming SUPPORT presentations? Please send it to me

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Nguyen, Cuong \(NIH/NHLBI\) \[E\]](#)
To: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#); [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: logo
Date: Friday, April 23, 2010 11:36:50 AM
Attachments: [StandardSignature_CMYK.jpg](#)

Dear All,

Logo is attached.

Cuong

From: Blaisdell, Carol (NIH/NHLBI) [E]
Sent: Friday, April 23, 2010 11:34 AM
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Cc: Nguyen, Cuong (NIH/NHLBI) [E]
Subject: RE: logo

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Subject: logo

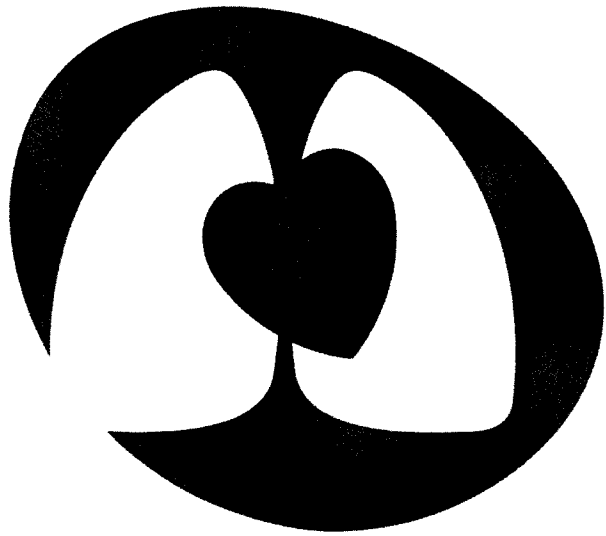
Carol

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Thanks

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higginsr@mail.nih.gov



National **Heart**
Lung and Blood Institute

From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [Nguyen, Cuong \(NIH/NHLBI\) \[E\]](#)
Subject: RE: logo
Date: Friday, April 23, 2010 11:34:14 AM
Attachments: [NHLBI title slide.ppt](#)

Rose,

For your presentation at Pediatric Academic Society meeting next week,

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Cuong who works with our lung division director may have other ideas.

cb

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 10:27 AM
To: Blaisdell, Carol (NIH/NHLBI) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: logo

Carol

Do you have an NHLBI logo that we could insert onto a POWERPOINT slide for the upcoming SUPPORT presentations? Please send it to me

Thanks

Rose

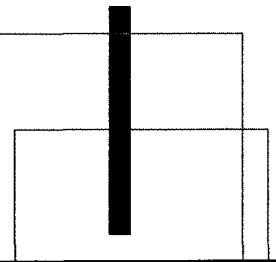
Rosemary D. Higgins, MD
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higginsr@mail.nih.gov



U.S. Department of Health and Human Services
National Institutes of Health



**National Heart
Lung and Blood Institute**





National Heart
Lung and Blood Institute

From: Niki Stratis
To: Alan Jobe; Anne Lee Solevag; Annie Janvier; Berit Holthe Munkeby; Berndt Uriesberger; Bob Lynch; Brett Manley; Britt Nakstad; Charles Christoph Roehr; Chris Beaumont; Christoph Huenseler; Claus Klingenberg; Colin Morley; Daniel Draper (for Gerald Hunt); Edgardo Szyld; Fernando Martinez (for Neil Finer); Fiona Wood; Georg Schmoelzer; Gerald Hunt; Gianluca Lista; Graeme Polglase; Hany Aly; Helene Osterholt; Helmut Hummler; Henrik Verder; Ingrid Dannevig; Jack Rabi; Jane Pillow; Jeff Perlman; Jennifer Dawson; Jessica Faenza (for Thorsten Waloschek and Bob Lynch); Jo Kexel (for Michael O'Reilly); John Kattwinkel; Karen Kirby (for Myra Wyckoff); Karen Link (for Alan Jobe); Keith Barrington; Khalid Aziz; Lex Doyle; Wright, Linda (NIH/NICHD) [C]; Lou Halamek; Maria Fernanda Almeida; Marilyn Escobedo; Mario Rojas; Martin Leckie; Masanori Tamura; Max Vento; Max Vento; Megan Wallace; Michael O'Reilly; Michael O'Reilly; Mike Meyer; Myra Wyckoff; Nalini Singhal; Neil Finer; Noah Hillman; Ola Saugstad; Omar Kamlin; Stonebanks, Paula (NIH/NICHD) [E]; Paulina Toso; Peter Davis; Richard Martin; Robert Kopotic; Ronnaug Solberg; Higgins, Rosemary (NIH/NICHD) [E]; Ruth Guinsburg; Stuart Hooper; Suhas Kallapur; Susan Niermeyer; Thorsten Waloschek; Tina Leone; Raju, Tonse (NIH/NICHD) [E]; Wade Rich
Subject: FINAL PROGRAM - 2nd Neonatal Resuscitation Research Workshop
Date: Friday, April 23, 2010 2:23:51 AM
Attachments: PROGRAM.doc

Dear Colleagues

Please find attached the FINAL program for the 2nd Neonatal Resuscitation Research Workshop.

Niki Stratis
Assistant to Professor/Director of Neonatal Medicine
Newborn Research
Level 7, Room 166
The Royal Women's Hospital
20 Flemington Road
Parkville Vic 3052
Australia
Phone: + 613 8345-3763
Fax: + 613 8345-3789
E-mail: niki.stratis@thewomens.org.au

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9.00 – 9.20 am

Jane Hillow

Implications of hypo and hyperthermia for the preterm lung during initiation of ventilation.

9.20 – 9.40 am

Masanori Tamura

Different ways of tracheal suction to prevent MAS.

9.40 – 10.00 am

MORNING TEA – Quarter Deck and Bridge

10.00 – 10.20 am (Chairperson: John Kattwinkel)

Susan Niermeyer

Field testing of global educational program for neonatal resuscitation.

10.20 – 10.40 am

Ruth Guinsburg

Deaths up to 6 days after birth associated with intrauterine hypoxia or asphyxia in Brazil: a 2005-2007 national study.

10.40 – 11.00 am

Rosemary Higgins

Challenges and opportunities for research in the Neonatal Research Network.

11.00 – 11.20 am

Maria Fernanda Branc de Almeida

Hypothermia in preterm newborn infants <34 weeks born in the Brazilian Neonatal Network: a prospective study from delivery room to NICU admission.

11.20 – 11.40 am

Brett Manley

Clinical assessment of extremely premature infants in the delivery room is a poor predictor of survival.

11.40 – 12.30 pm

LUNCH – Dockside Restaurant

12.30 – 12.50 pm (Chairperson: Myra Wyckoff)

Stuart Hooper

Cardiovascular transition at birth and the potential benefit of delayed cord clamping.

12.50 – 1.10 pm

Chalid Aziz

Practical application of delayed cord clamping.

1.10 – 1.30 pm

Marilyn Escobedo

Echocardiographic studies in transitional circulation.

1.30 – 1.50 pm

Michael Meyer

SVC flow and cord clamping.

1.50 – 2.10 pm

AFTERNOON TEA – Quarter Deck and Bridge

2.10 – 2.30 pm (Chairperson: Susan Niermeyer)

Lou Halamek

Value of simulation and debriefing in neonatal resuscitation.

2.30 – 2.50 pm

Wade Rich

The problems of antenatal consent in delivery room RCTs.

2.50 – 3.10 pm

Myra Wyckoff

Impact of delivery room CPR on the outcome of preterm infants.

3.10 – 3.30 pm

Anne Lee Solevag

What is the optimal compression ventilation ratio?

3.30 – 3.50 pm

Late Afternoon Tea – Quarter Deck and Bridge

3.50 – 4.10 pm

Ingrid Dannevig

Can the number of newborns receiving cardiac compressions be reduced?

4.10 – 4.30

Colin Morley

Personal views of 40 years of neonatal resuscitation.

4.30 – 4.50 pm

Alan Jobe

Send us away wiser.

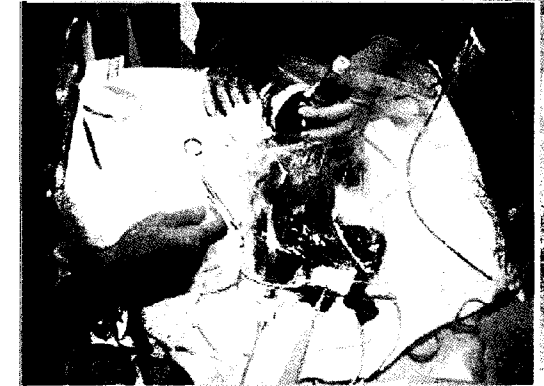
7.30 pm

DINNER – Dockside Restaurant

2nd Neonatal Resuscitation

Research Workshop

4th - 6th May 2011



Quarter Deck and

Bridge Rooms

The Granville Island Hotel

1253 Johnston Street

Vancouver, BC

Canada

Fisher & Paykel
HEALTHCARE

NHMRC CCRC
in
Newborn Medicine

MASIMO
Dräger

Tuesday 4th May

7.30 pm Welcome Dinner
Dockside Restaurant
The Granville Island Hotel

Wednesday 5th May

8.00 – 8.10 am (Chairperson: Richard Martin)

Colin Morley
Welcome and why are we here?

8.10 – 8.30 am
Ola Saugstad
Metabolomic analyses of plasma. New insights into asphyxia and resuscitation in pigs.

8.30 – 8.50 am
Max Vento
Oxidative stress.

8.50 – 9.10 am
Hany Aly
Oxygen toxicity from mother to baby.

9.10 – 9.30 am
Neil Finer
SUPPORT trial report of oxygen arm.

9.30 – 9.50 am
Annie Janvier
Clinical ethics orientated resuscitation research.

9.50 – 10.10 am
MORNING TEA – Quarter Deck and Bridge

10.10 – 10.30 am (Chairperson: Keith Barrington)
Jennifer Dawson
SpO₂ and heart rate centiles in the delivery room – how should they be used?

10.30 – 10.50 am
Robert Kopotic
Comparison of cerebral and pulse oximetry.

10.50 – 11.10 am
Heimut Hummler
Brain tissue oxygenation during resuscitation.

11.10 – 11.30 am
Berndt Urlesberger
Regional oxygen saturation of the brain differs from peripheral tissue during transition of the newborn.

11.30 – 11.50 am
Richard Martin
Intermittent hypoxic episodes as an oxidant stress.

11.50 am – 12.10 pm
Wade Rich, Neil Finer or Max Vento
The PreSox trial.

12.10 pm
LUNCH – Dockside Restaurant

1.00 – 1.20 pm (Chairperson: Jeff Perlman)
Stuart Hooper
Facilitating lung aeration at birth.

1.20 – 1.40 pm
Claus Klingenberg
Devices for delivering sustained inflations.

1.40 – 2.00 pm
Edgardo Szyld
Study comparing a T piece vs a self inflating bag.

2.00 – 2.20 pm
Megan Wallace
Effect of a sustained inflation on markers of lung injury.

2.20 – 2.40 pm
Gianluca Lista
Sustained lung inflation in the delivery room: personal experience.

2.40 – 3.00 pm
Afternoon Tea – Quarter Deck and Bridge

3.00 – 3.20 pm (Chairperson: Peter Davis)
Tina Leone
End tidal CO₂ and ventilation in the delivery room.

3.20 – 3.40 pm
Georg Schmoelzer
Monitoring of respiratory function after birth: use of a Respiratory Function Monitor.

3.40 – 4.00 pm
John Kattwinkel
Effect of changing compliance on tidal volume delivery.

4.00 – 4.20 pm
Christoph Huenseler
Surfactant delivery through a thin catheter.

4.20 – 4.40 pm
Mario Rojas
Very early surfactant and nCPAP in the delivery room.

4.40 – 5.00 pm
Late Afternoon Tea – Quarter Deck and Bridge

5.00 – 5.20 pm
Neil Finer
The SUPPORT study – CPAP arm.

5.20 – 5.40 pm
Henrik Verder
Prediction (at birth) of RDS and which babies should receive surfactant.

5.40 – 6.00 pm
Thorsten Waloscheck
The Baby First initiative.

7.30 pm
Dinner – Dockside Restaurant

Thursday 6th May

8.00 – 8.20 am (Chairperson: Alan Jobe)
Graeme Polglaze
Effect of inflammation and ventilation on cerebral hemodynamics and injury.

8.20 – 8.40 am
Noah Hillman
Inflammatory progression after stretch injury of the fetal airway.

8.40 – 9.00 am
Suhas Kallapur
Modulation of inflammation – implications for resuscitation injury.

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; "Wally Carlo, M.D."
Subject: RE: Carlo OA Galleys
Date: Thursday, April 22, 2010 2:00:23 PM

Adobe puts little blue editing carets in the text. If you move the cursor over them, you should see a pop-up with the names to be inserted. I can't see any way to make the popup boxes remain on the page all the time.

When the NEJM editors see it, they should be able to move through the document from one edit mark to another and accept or reject them, in the same way you can when you use Track Changes in Word.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 1:48 PM
To: Archer, Stephanie (NIH/NICHD) [E]; 'Wally Carlo, M.D.'
Subject: RE: Carlo OA Galleys

I can't see the additional boilerplate names for Case, Brown and Dallas? How does the document get 'viewed' to see these??

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 1:42 PM
To: 'Wally Carlo, M.D.'
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Carlo OA Galleys

Attached is a version with the boilerplate and author changes in it. Let me know if you need any additional help.

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, April 22, 2010 1:12 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Carlo OA Galleys

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

From: NEJM Galleys [mailto:NejmGalleys@mms.org]
Sent: Tuesday, April 20, 2010 2:04 PM
To: Wally Carlo, M.D.
Subject: Carlo OA Galleys

PLEASE DO NOT REPLY TO THIS E-MAIL

AUTHOR: Carlo

MANUSCRIPT EDITOR: Sharon Hogan (shogan@nejm.org); (800) 445-8080 or (617) 734-9800

Please check the attached galley proofs of your article

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If you have already made arrangements with Sharon Hogan to go over your galley changes, please call her at 800-445-8080 or 617-734-9800 at the time you have set up. If you cannot reach this Manuscript Editor, telephone our Manuscript Editing Department at 800-445-8080 or 617-734-9800 **no later than noon on Monday, April 26, 2010.**

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From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; "Wally Carlo, M.D."; Finer, Neil; Das, Abhik; Gantz, Marie
Subject: RE: Carlo galleys - changes
Date: Thursday, April 22, 2010 1:45:35 PM

Please ignore my earlier email and use the version that Rose sent out. The names for Duke and Emory were for people on the ROP Adjudication Committee, so they are listed at the end of the Acknowledgements section - they do NOT need to be in two places.

I have sent Wally a version of the PDF with the requested changes in it.

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 8:55 AM
To: 'Wally Carlo, M.D.'; Finer, Neil; Das, Abhik; Gantz, Marie
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: Carlo galleys - changes

Here are the changes to authorship/boilerplate.

Thanks
Rose

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS
Date: Thursday, April 22, 2010 12:47:00 PM

She has NEI and NICHD in the acknowledgement section of her poster so she is good to go

Rose

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 11:49 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

I saved these under the Template subfolder on the N:\ drive. Should we also have a NEI logo on Dale's presentation? If so, any idea who I should contact for it?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 10:35 AM
To: 'Finer, Neil'; 'Wally Carlo, M.D.'
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

Here are the logos – a simple statement saying NHLBI and NICHD funded the study is fine.

I have attached two logos and have asked Carol Blaisdell for one that is POWERPOINT friendly in case these don't work

Rose

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Thursday, April 22, 2010 10:35 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; 'Wally Carlo, M.D.'
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

Rose

Can you send me a logo for the NHLBI and whether you want to say anything
We did not specifically mention any grant support on the presentation – What do you want to say
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center

402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, April 22, 2010 7:26 AM
To: 'Wally Carlo, M.D.'; Finer, Neil
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT PRESENTATIONS FOR PAS AND ATS

Hi,

For the platform presentations, we need to acknowledge NHLBI's funding for SUPPORT either on the title slide or on the slide that lists the NRN centers. Let me know if you want us to fix either of these slides in your presentations. Sorry I didn't pick this up earlier, but we must acknowledge them!!!

Let me know if you want our assistance.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; "Wally Carlo, M.D."; Finer, Neil; Das, Abhik; Gantz, Marie
Subject: RE: Carlo galleys - changes
Date: Thursday, April 22, 2010 12:02:34 PM
Attachments: Carlo, SUPPORT, galleys, 2010-04-21 changes.doc

Please use this version of changes instead - it includes a few more missing names for Duke and Emory.

Thanks,

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, April 22, 2010 8:55 AM
To: 'Wally Carlo, M.D.'; Finer, Neil; Das, Abhik; Gantz, Marie
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: Carlo galleys - changes

Here are the changes to authorship/boilerplate.

Thanks
Rose

Wally

The following changes need to be made:

1. WR [Wade Rich] should be UCSD, not UAB on title page.
2. Stephanie tells me that Pablo and Anthony Pizza should have the order changed (Piazza before Sanchez based on recruitment). I apologize this was not picked up sooner.
3. Brown acknowledgements – **please add:** Susan Barnett, RRT; Sarah Lillie, RRT
4. Case acknowledgements – **please add:** Arlene Zadell RN; Julie DiFiore, BS.
5. Duke acknowledgements – **please add:** David K. Wallace, MD MPH; Sharon F. Freedman, MD.
6. Emory acknowledgements – **please add:** Amy K. Hutchinson, MD.
7. University of Rochester acknowledgements – please add: Gary D. Markowitz, MD.
8. UT Southwestern Acknowledgement – **please add:** James Allen, RRT; Laura Grau, RN; Melissa Martin, RN; Araceli Solis, RRT; Diana M. Vasil, RNC-NIC; Kerry Wilder, RN.
9. For the grant number paragraph, use the following:

Supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (Grant numbers: U10 HD21364, U10 HD21373, U10 HD21385, U10 HD21397, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27871, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40461, U10 HD40492, U10 HD40498, U10 HD40521, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD53119, U10 HD53124), co-funding from the National Heart, Lung, and Blood Institute, and grants from the National Institute of Health (Grant numbers: M01 RR30, M01 RR32, M01 RR39, M01 RR44, M01 RR54, M01 RR59, M01 RR64, M01 RR70, M01 RR80, M01 RR125, M01 RR633, M01 RR750, M01 RR997, M01 RR6022, M01 RR7122, M01 RR8084, M01 RR16587, UL1 RR25008, UL1 RR24139, UL1 RR24979, UL1 RR25744).

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@nih.gov)
To: "Finer, Neil"; "Wally Carlo, M.D."
Cc: [Archer, Stephanie \(NIH/NICHD\) \[E\]](mailto:Archer.Stephanie@nih.gov)
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS
Date: Thursday, April 22, 2010 11:05:00 AM

This looks fine

Thanks
Rose

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Thursday, April 22, 2010 10:51 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; 'Wally Carlo, M.D.'
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

Hi Rose
Have a look at how I did this
I also changed the last slide
I will take full responsibility for the wording
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
UC San Diego Medical Center
402 Dickinson Street, MPF 1-140
San Diego, CA 92103
Telephone: 619-543-3759
Facsimile: 619-543-3812

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Thursday, April 22, 2010 7:35 AM
To: Finer, Neil; 'Wally Carlo, M.D.'
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

Here are the logos – a simple statement saying NHLBI and NICHD funded the study is fine.
I have attached two logos and have asked Carol Blaisdell for one that is POWERPOINT friendly in case these don't work

Rose

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]

Sent: Thursday, April 22, 2010 10:35 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; 'Wally Carlo, M.D.'
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS

Rose

Can you send me a logo for the NHLBI and whether you want to say anything
We did not specifically mention any grant support on the presentation – What do you want to say
Neil

Neil N. Finer, M.D.
Professor of Pediatrics
Director, Division of Neonatology
Department of Pediatrics
UC San Diego School of Medicine
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From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, April 22, 2010 7:26 AM
To: 'Wally Carlo, M.D.'; Finer, Neil
Cc: Archer, Stephanie (NIH/NICHD) [E]
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Rosemary D. Higgins, MD
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"; "Wally Carlo, M.D."
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT PRESENTATIONS FOR PAS AND ATS
Date: Thursday, April 22, 2010 10:34:00 AM
Attachments: [NHLBI black and white logo.jpg](#)
[NHLBI color logo.jpg](#)

Here are the logos – a simple statement saying NHLBI and NICHD funded the study is fine.

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Rose

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Cc: Archer, Stephanie (NIH/NICHD) [E]
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Neil

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Sent: Thursday, April 22, 2010 7:26 AM
To: 'Wally Carlo, M.D.'; Finer, Neil
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT PRESENTATIONS FOR PAS AND ATS

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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
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301-496-3790 (FAX)
higginsr@mail.nih.gov





From: Caplan, Michael
To: Higgins, Rosemary (NIH/NICHD) [E]; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Zaterka-Baxter, Kristin
Subject: RE: PAS oxygen symposium
Date: Wednesday, April 21, 2010 4:32:22 PM

I think Wally will need oxygen to start his presentation at 6 am....

Best of luck

mickey

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, April 21, 2010 3:30 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Caplan, Michael; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Zaterka-Baxter, Kristin
Subject: PAS oxygen symposium

Hi

Wally Carlo was asked to present the SUPPORT oximetry results at an oxygen symposium at 6 – 8 am on Monday may 3 – he will use the same slides as he uses on Sunday at PAS.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
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301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: conference call
Date: Wednesday, April 21, 2010 4:32:10 PM

OK. How about if I reserve the conference line for 1 p.m.?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, April 21, 2010 4:31 PM
To: Bock, Robert (NIH/NICHD) [E]
Subject: conference call

Bob
Wally Carlo and Neil Finer are available on 5/12 between 1230 -4 PM ET.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Kristi Watterberg
To: Oh William (E-mail); Nancy Newman; Ed Donovan; Kurt Schibler [kurt.schibler@cchmc.org]; Vivek Narendran; Brad Yoder (Bradley.yoder@hsc.utah.edu); Roger Faix; Brenda Poindexter; Krisa VanMeurs; Higgins, Rosemary (NIH/NICHD) [E]; cotte010@mc.duke.edu; Ronald Goldberg; Shahnaz "Duara; Beena" "Sood; Seetha Shankaran; "BrendaMorris"; Mickey Caplan; Anthony Piazza(Anthony.Piazza@oz.ped.emory.edu); Stoll Barbara (E-mail); (susie.buchter@oz.ped.emory.edu); CarloWaldemar (E-mail); aaf2@po.cwru.edu; Michelle Walsh; Abhik Das; Dennis Wallace; Marie Gantz; Poole Kenneth (E-mail); Stevenson David (E-mail); Ivan Frantz(ifrantz@tuftsmedicalcenter.org); Ambal (ambal@uab.edu); Neil Finer; Wade "Rich; Ed Bell; (rohls@unm.edu); Dale "Phelps; Nirupama Laroia; Tyson Jon (E-mail); Kathleen A Kennedy; (Luc.Brion@UTSouthwestern.edu); Pablo Sanchez; "MichaelO`Shea"; alaptook@WIHRI.org; Matthew Bizzarro; EhrenkranzRichard (E-mail); "vineet.bhandari@yale.edu"
Cc: Archer, Stephanie (NIH/NICHD) [E]; Kristin "Zaterka-Baxter; Meg Cunningham; Carolyn Petrie "Huitema
Subject: Re: ****CONFIDENTIAL UPDATE ON SUPPORT PAPERS*****
Date: Wednesday, April 21, 2010 2:59:19 PM

Fantastic news - congratulations!! Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 4/21/2010 8:46 AM >>>

Hi,

We have been informed by NEJM that both SUPPORT Papers will be accelerated Online First release scheduled to coincide with the presentations of the results at the American Thoracic Society's annual meeting on Sunday May 16, 2010. The on-line release will occur at 1 PM EDT on 5/16/2010. The print publication is slated to appear in the May 27, 2010 issue of NEJM.

As far as I know, this will be a first for the Neonatal Research Network.

The SUPPORT abstracts will be presented in platforms at PAS. Neil will deliver the same talks will be given at a post-PAS meeting on neonatal resuscitation.

We are not to discuss the fact that the papers have been reviewed or accepted by NEJM. PI's - please insure that all of your staff with the confidential knowledge regarding the SUPPORT papers are aware of the NEJM rules!! This is particularly important for those attending the PAS meeting who may be asked about the status of the papers. **If asked, the appropriate response is "The manuscripts are in the peer review process."**

In addition, since the papers are not yet published in NEJM, we need to respect their embargo policy. This means that we are requested to follow the guidelines at <http://authors.nejm.org/Help/Embargo.asp>.

Specifically, the guidelines state:

- Please do not discuss the fact that the research has been submitted or accepted for publication in the *New England Journal of Medicine*.
- Please do not distribute any copies of the manuscript, tables, or figures. (It is acceptable to use the materials in a presentation, but they should not be distributed.)

**THANKS TO ALL OF YOU AND YOUR STAFF FOR THE
EFFORT INVOLVED IN THIS LANDMARK STUDY.**

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: NHLBI contacts for SUPPORT
Date: Wednesday, April 21, 2010 1:57:06 PM

Thanks Rose.

Carol J. Blaisdell, M.D.
Medical Officer
Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Sent: Wednesday, April 21, 2010 1:53 PM
To: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
Cc: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#); [Gail, Dorothy \(NIH/NHLBI\) \[E\]](#)
Subject: NHLBI contacts for SUPPORT

Bob

I have the contact info above for the NHLBI program folks for the SUPPORT Trial.
They can also review the press release

Regards
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#); [Gail, Dorothy \(NIH/NHLBI\) \[E\]](#)
Subject: RE: NHLBI contacts for SUPPORT
Date: Wednesday, April 21, 2010 1:54:17 PM

Hello. I sent a copy of our release to Susan Dambrauskas and Diane Striar. I expect one of them will be contacting you shortly. If you need it, I'm also happy to send you a copy directly.

Just let me know.

Thanks.

Bob

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Sent: Wednesday, April 21, 2010 1:53 PM
To: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
Cc: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#); [Gail, Dorothy \(NIH/NHLBI\) \[E\]](#)
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higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#); [Gail, Dorothy \(NIH/NHLBI\) \[E\]](#)
Cc: [Spong, Catherine \(NIH/NICHD\) \[E\]](#)
Subject: SUPPORT
Date: Tuesday, April 20, 2010 2:59:09 PM

Hi,

We were informed this afternoon by NEJM that there will be an on-line release of both support papers at 1 pm on 5/16 to coincide with the ATS presentation. The papers will appear in print in the 5/27 issue.

I am on leave today but will be in the rest of the week. I am happy to discuss.

Thanks so much for your incredible support for this study!!

Best regards

Rose

From: Roger Faix
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT
Date: Monday, April 19, 2010 4:39:42 PM

Thanks, Rose!

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Monday, April 19, 2010 2:38 PM
To: Roger Faix; Bradley Yoder; 'Anna Bodnar'; Karen Osborne RN
Cc: Gantz, Marie
Subject: SUPPORT

CONGRATULATIONS.

We have no missing SUPPORT FU outcomes currently from your site. Keep of the excellent work and thanks for all the effort!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Gantz, Marie"
Cc: "Das, Abhik"
Subject: RE: SUPPORT missing FU
Date: Monday, April 19, 2010 4:39:00 PM

All have been sent – we are doing quite well in this trial – high FU RATE!!!!

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Friday, April 16, 2010 12:32 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: SUPPORT missing FU

Rose,

Attached is the list of SUPPORT infants missing FU this month.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Roger Faix"; "Brad Yoder (Bradley.yoder@hsc.utah.edu)"; "Anna Bodnar"; "Karen Osborne RN"
Cc: "Gantz, Marie"
Subject: SUPPORT
Date: Monday, April 19, 2010 4:38:00 PM
Importance: High

CONGRATULATIONS.

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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ehrenkranz Richard (E-mail)"; "monica.konstantino@yale.edu"; "elaine.romano@yale.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT
Date: Monday, April 19, 2010 4:37:00 PM
Importance: High

CONGRATULATIONS.

We have no missing SUPPORT FU outcomes currently from your site. Keep of the excellent work and thanks for all the effort!!!

Rose

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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo Sanchez"; "Roy Heyne"; "Nancy Miller"; "Diana Vasil"; "Lizette Torres"
Cc: "Gantz, Marie"
Subject: SUPPORT
Date: Monday, April 19, 2010 4:36:00 PM
Importance: High

CONGRATULATIONS.

We have no missing SUPPORT FU outcomes currently from your site. Keep of the excellent work and thanks for all the effort!!!

Rose

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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mcw3@case.edu"; "Nancy Newman"; "Bonnie Siner"; "drfjcmd@aol.com"
Cc: "Gantz, Marie"
Subject: SUPPORT
Date: Monday, April 19, 2010 4:36:00 PM
Importance: High

CONGRATULATIONS.

We have no missing SUPPORT FU outcomes currently from your site. Keep of the excellent work and thanks for all the effort!!!

Rose

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From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: "[Finer, Neil](#)"
Subject: PAS
Date: Monday, April 19, 2010 3:18:00 PM

The SUPPORT platform presentation has gone through NICHD clearance with no further suggestions. You can upload the slides.

Thanks
Rose

Rosemary D. Higgins, MD
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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Hanson, James (NIH/NICHD) [E]
Subject: RE: Press release for SUPPORT TRIAL
Date: Monday, April 19, 2010 11:02:00 AM

THANKS

Also – nice to see you last night!!!
We were returning from the chorus trip!!
Rose

From: Hanson, James (NIH/NICHD) [E]
Sent: Monday, April 19, 2010 11:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Press release for SUPPORT TRIAL

Yes

Sent from my BlackBerry Wireless Handheld (www.BlackBerry.net)

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Hanson, James (NIH/NICHD) [E]
Sent: Mon Apr 19 09:05:47 2010
Subject: Press release for SUPPORT TRIAL

Jim -

I know you are travelling – did you have a chance to review the press release for the SUPPORT Study?

Thanks
Rose

Rosemary D. Higgins, MD
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From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Interview Request: Supplemental oxygen therapy in premature infants with modest ROP
Date: Monday, April 19, 2010 10:35:37 AM

Hi Rose. Are you in the office today?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Monday, April 19, 2010 10:21 AM
To: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview Request: Supplemental oxygen therapy in premature infants with modest ROP

NEI was NOT involved in our SUPPORT study- also, we have not gotten a publication date – How should we proceed??

If this is another paper, I could comment

Rose

From: Bock, Robert (NIH/NICHD) [E]
Sent: Monday, April 19, 2010 10:19 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Interview Request: Supplemental oxygen therapy in premature infants with modest ROP

FYI.

From: Balintfy, Joseph (NIH/OD) [E]
Sent: Monday, April 19, 2010 10:18 AM
To: HHS/OS Interviews
Cc: Burklow, John (NIH/OD) [E]; Allen, Marin (NIH/OD) [E]; Ralbovsky, Don (NIH/OD) [E]; Carper, Deborah (NIH/NEI) [E]; Collins, Allyson (NIH/NEI) [E]; Collins-Lee, Kym (NIH/NEI) [E]; Harper, Anna (NIH/NEI) [E]; Horrigan, Jean (NIH/NEI) [E]; Janiszewski, Rosemary (NIH/NEI) [E]; Walls, Sherrita (NIH/NEI) [C]; Bock, Robert (NIH/NICHD) [E]
Subject: Interview Request: Supplemental oxygen therapy in premature infants with modest ROP

Jacqueline Salmon
Pew Charitable Trust
Subject: Supplemental oxygen therapy in premature infants with modest Retinopathy of Prematurity
Deadline: today

Spokesperson: Dr. Brian Brooks, Staff Clinician, NEI Clinic

Ms. Salmon is writing a report for the Pew Charitable Trust's board members. Dr. Brooks will discuss the findings of NEI's study on administering supplemental oxygen to premature infants with pre-threshold cases of retinopathy of prematurity (ROP). The study found that modest supplemental oxygen given to premature infants with moderate cases of ROP, may not significantly improve ROP, but definitely does not make it worse.

From: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
To: [Susan Hintz](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Hintz, SUPPORT Neuroimaging, 2010-04-19 swa.ppt
Date: Monday, April 19, 2010 9:48:57 AM
Attachments: [Hintz, SUPPORT Neuroimaging, 2010-04-19 swa.ppt](#)

Hi Susan,

I combined the two acknowledgements slides in your presentation (attached), and only showed the centers that recruited into SUPPORT MRI.

Stephanie



Early and Late CUS Findings in the SUPPORT Neuroimaging and Neurodevelopmental Outcomes (NEURO) Cohort

SR Hintz, D Bulas, TL Slovis, H Cheng, N Finer, A Das,
RD Higgins, SUPPORT Subcommittee, for NICHD
Neonatal Research Network



Lucile Packard Children's Hospital

STANFORD UNIVERSITY MEDICAL CENTER



Disclosure

- The presenter, Susan R. Hintz, M.D., has no conflicts to disclose



Cranial US

- Cranial US is a crucial neuroimaging tool, current standard of care for preterm infants.
 - Ment LR, et. al. *Neurology* 2002; 58:1726
- CUS findings are used to assist in prognosis of neurodevelopmental outcomes.
- Data regarding CUS findings and childhood outcomes in recent extremely preterm cohorts are essential.
 - O'Shea TM, et. al. *Pediatrics* 2008;122:e662; Kuban KCK, et. al. *J Child Neurol* 2009;24:63



Objective

- In the NEURO subcohort of the NICHD Neonatal Research Network Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT), we determined:
 - **Early and late CUS findings**
 - **Inter-rater reliability between central readers**
 - **Accuracy of local readings compared with central readings**



SUPPORT Study

- SUPPORT was a randomized, multicenter trial of ventilation and oxygenation strategies in 24-27+6/7 week EGA infants; interventions began in the delivery room.
 - **SUPPORT results will be presented:**
 - May 1, 2:45 pm. Neonatal Medicine: Clinical Trials (Neil Finer)
 - May 2, 4:15 pm. Perinatal Epidemiology (Wally Carlo)



Methods: NEURO Study

- Prospective study of **early CUS** (4-14 days) and **late CUS** (35-42 weeks PMA) in a subcohort of SUPPORT
 - NEURO study also obtained brain MRI within 5 days of late CUS
 - Neurodevelopmental follow-up will occur at 18-22 months and 6 ½ to 7 ½ years



Methods: Patients and Enrollment

- 16 Neonatal Research Network sites participated in NEURO secondary
- Sites implemented secondary enrollment strategy best suited for their center
 - Consent with or after main trial consent
- NEURO launched after main trial start
 - IRB processes, neuroradiology arrangements for MRI portion of this study



Methods: Imaging and Local Reading

- NEURO protocol called for two CUS:
 - **Early:** 4-14 days of age
 - **Late:** 35-42 weeks PMA
- CUS views and planes obtained per local site clinical protocol; local readings per local clinical approach
- Trained research personnel at each site collected hemisphere-specific data from local radiologists' reports to NEURO study form



Methods: Central Reading

- Copies of early and late CUS sent by centers to RTI International (data center)
- Two masked central readers interpreted CUS during two 2-day reading sessions
- Central reader form collected detailed hemisphere-specific radiologic observations and diagnostic data
 - Hintz SR, et. al. *J Pediatr* 2007;150:592



Methods: Analysis

- Reliability analysis by kappa statistic
 - $\text{Kappa} = \frac{\% \text{ observed agreement} - \% \text{ expected agreement}}{100\% - \% \text{ expected agreement}}$
 - ≥ 0.75 considered “substantial” to “excellent” agreement
- Accuracy analysis by sensitivity and specificity
 - Each central reader as “gold standard” against which local reader was compared

Fleiss JL, Statistical Methods, 1981; Landis JR, Biometrics, 1977



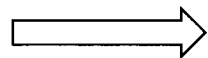
Results: Cohort and CUS scans

- **572 infants with early and late CUS**
- Early CUS obtained at $8_{\pm}4$ days of age
 - Median: 7 days
- Late CUS obtained at $37_{\pm}2$ weeks PMA
 - Median: 37 weeks PMA



Baseline Characteristics

N	572
BW, mean (SD)	848 (190) grams
EGA, mean (SD)	25.9 (1) weeks
Multiple gestation	23%
Male	56%
Race	
Non-Hispanic Black	30%
Non-Hispanic White	43%
Male	56%
Antenatal steroids	95%
Cesarean section	69%
Apgar score <3 at 5 minutes	3%
Maternal education < HS	21%



Central reader findings: **Early CUS**

	Central Reader 1	Central reader 2
EARLY CUS findings		
	N=572	N=572
Normal	72.0%	71.7%
Normal or choroid plexus bleed/cyst only	74.6%	72.6%
Any GMH or IVH	19.6%	20.8%
Grade 1 or 2	14.2%	12.2%
Grade 3 or 4	6.8%	9.6%
Any ventricular enlargement	8.8%	9.4%
Moderate-severe ventricular enlargement	4.6%	4.6%
PVL (echodense or echolucent)	1.1%	0.5%
Cerebellar/posterior fossa lesion	1.6%	1.2%



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Central reader findings: Late CUS

	Central Reader 1	Central Reader 2
LATE CUS findings		
	N=571	N=572
Normal	70.8%	70.6%
Normal or choroid plexus bleed/cyst only	75.0%	73.1%
Any ventricular enlargement	7.7%	8.4%
Moderate-severe ventricular enlargement	4.4%	4.2%
Echolucent PVL (cPVL)	1.6%	1.1%
Porencephalic cyst (P-cyst)	2.1%	2.6%
cPVL or P-cyst or any ventriculomegaly or shunt	9.1%	9.6%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	6.5%	6.6%
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cPVL or P-cyst or any ventriculomegaly or shunt	9.1%	9.6%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	6.5%	6.6%
Cerebellar/posterior fossa	1.1%	0.4%



Progression of Findings

- Of those with **normal early CUS**
 - ~80% remained **normal** on late CUS
 - 81% central reader 1; 82% central reader 2
 - Only 1% had moderate-severe ventriculomegaly on late CUS
- Of those with **grade 3 or 4** on early CUS
 - ~25% progressed to porencephalic cyst on late CUS
 - 26% central reader 1; 25% central reader 2



Central Reader Reliability: Early CUS

	Kappa	95% CI	PPA
EARLY CUS			
Normal vs. abnormal	0.76	(0.70, 0.82)	93%
Any GMH or IVH	0.79	(0.73, 0.85)	81%
Grade 1 or 2	0.52	(0.43, 0.61)	56%
Grade 3 or 4	0.77	(0.67, 0.87)	74%
Grade 3 or 4 or cPVL	0.75	(0.65, 0.85)	73%
Moderate-severe ventricular enlargement	0.84	(0.73, 0.95)	85%
PVL (echodense or echolucent)	0.22	(-0.15, 0.58)	22%



Central Reader Reliability: Late CUS

	Kappa	95% CI	PPA
LATE CUS			
Normal vs. abnormal	0.66	(0.59, 0.73)	90%
ANY ventricular enlargement	0.88	(0.83, 0.94)	89%
Moderate-severe ventricular enlargement	0.90	(0.84, 0.97)	91%
Echolucent PVL (cPVL)	0.45	(0.19, 0.71)	46%
Porencephalic cyst (P-cyst)	0.76	(0.58, 0.93)	76%
cPVL or P-cyst or any ventriculomegaly or shunt	0.84	(0.79, 0.90)	86%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	0.88	(0.82, 0.94)	89%



Accuracy of Local Interpretation Early CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any ventricular enlargement	72.5%	97.1%	51.4%	97.2%
Any PVL	33.3%	98.2%	0%	97.9%



Accuracy of Local Interpretation Early CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any ventricular enlargement	72.5%	97.1%	51.4%	97.2%
Any PVL	33.3%	98.2%	0%	97.9%



Accuracy of Local Interpretation Late CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
Any ventricular enlargement	77.3%	96.2%	75.0%	96.5%
Cystic PVL (cPVL)	66.7%	98.4%	50.0%	97.9%
Porencephalic cyst (P-cyst)	50.0%	99.6%	33.3%	99.5%
cPVL or P-cyst or any ventriculomegaly or shunt	80.8%	95.0%	74.5%	94.7%



Accuracy of Local Interpretation Late CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
Any ventricular enlargement	77.3%	96.2%	75.0%	96.5%
Cystic PVL (cPVL)	66.7%	98.4%	50.0%	97.9%
Porencephalic cyst (P-cyst)	50.0%	99.6%	33.3%	99.5%
cPVL or P-cyst or any ventriculomegaly or shunt	80.8%	95.0%	74.5%	94.7%



Accuracy of Local Interpretation Late CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	85.5%	59.9%	85.3%	58.9%
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Summary

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 - Central reader reliability and local reader accuracy were very good for major adverse or composite CUS findings
 - Poorer for normal late CUS and rare findings, poorer reliability for lower grade hemorrhage



Discussion

- This study did not include local radiologist training or require specific CUS views
- Only two protocol scans obtained
- Unique cohort, part of a multicenter trial; therefore, results may not be generalizable
 - Despite limitations, NEURO will be the largest extremely preterm cohort to date with CUS, brain MRI, and long-term follow-up; likely not possible outside of a multicenter network



Discussion

- CUS were normal in ~70% of this cohort
 - But this does not assure normal outcome
 - O'Shea TM, et. al. *Pediatrics* 2008; Broitman E, et. al. *J Pediatr* 2007; Laptok A, et. al. *Pediatrics* 2005
 - Brain MRI results may augment CUS findings
- NEURO study will assess value of CUS and MRI, alone and with other risk factors, to predict neurologic and cognitive outcomes in early and later childhood



NICHD Neonatal Research Network

- **Special thanks to**
 - NRN site Coordinators
 - Meg Cunningham
 - Kris Zaterka
 - Carolyn Petrie-Huitema
 - Amanda Irene
 - Julie Croxford



NICHD



NICHD Neonatal Research Network Centers (2005-2009)

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- RTI International
- Stanford University
- Tufts Medical Center
- University of Alabama – Birmingham
- University of California – San Diego
- University of Iowa
- University of New Mexico
- University of Rochester
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- University of Utah
- Wayne State University



NICHD



From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Subject: DRAFT_Rev0418_Hintz_NEURO_SUPPORT_cUS_PAS2010.ppt
Date: Monday, April 19, 2010 8:47:00 AM
Attachments: [DRAFT_Rev0418_Hintz_NEURO_SUPPORT_cUS_PAS2010.ppt](#)

For clearance



Early and Late CUS Findings in the SUPPORT Neuroimaging and Neurodevelopmental Outcomes (NEURO) Cohort

SR Hintz, D Bulas, TL Slovis, H Cheng, N Finer, A Das,
RD Higgins, SUPPORT Subcommittee, for NICHD
Neonatal Research Network



Lucile Packard Children's Hospital
STANFORD UNIVERSITY MEDICAL CENTER



Disclosure

- The presenter, Susan R. Hintz, M.D., has no conflicts to disclose



Cranial US

- Cranial US is a crucial neuroimaging tool, current standard of care for preterm infants.
 - Ment LR, et. al. *Neurology* 2002; 58:1726
- CUS findings are used to assist in prognosis of neurodevelopmental outcomes.
- Data regarding CUS findings and childhood outcomes in recent extremely preterm cohorts are essential.
 - O'Shea TM, et. al. *Pediatrics* 2008;122:e662; Kuban KCK, et. al. *J Child Neurol* 2009;24:63



Objective

- In the NEURO subcohort of the NICHD Neonatal Research Network Surfactant Positive Airway Pressure and Pulse Oximetry Trial (SUPPORT), we determined:
 - **Early and late CUS findings**
 - **Inter-rater reliability between central readers**
 - **Accuracy of local readings compared with central readings**



SUPPORT Study

- SUPPORT was a randomized, multicenter trial of ventilation and oxygenation strategies in 24-27+6/7 week EGA infants; interventions began in the delivery room.
 - **SUPPORT results will be presented:**
 - May 1, 2:45 pm. Neonatal Medicine: Clinical Trials (Neil Finer)
 - May 2, 4:15 pm. Perinatal Epidemiology (Wally Carlo)



Methods: NEURO Study

- Prospective study of **early CUS** (4-14 days) and **late CUS** (35-42 weeks PMA) in a subcohort of SUPPORT
 - NEURO study also obtained brain MRI within 5 days of late CUS
 - Neurodevelopmental follow-up will occur at 18-22 months and 6 ½ to 7 ½ years



Methods: Patients and Enrollment

- 16 Neonatal Research Network sites participated in NEURO secondary
- Sites implemented secondary enrollment strategy best suited for their center
 - Consent with or after main trial consent
- NEURO launched after main trial start
 - IRB processes, neuroradiology arrangements for MRI portion of this study



Methods: Imaging and Local Reading

- NEURO protocol called for two CUS:
 - **Early:** 4-14 days of age
 - **Late:** 35-42 weeks PMA
- CUS views and planes obtained per local site clinical protocol; local readings per local clinical approach
- Trained research personnel at each site collected hemisphere-specific data from local radiologists' reports to NEURO study form



Methods: Central Reading

- Copies of early and late CUS sent by centers to RTI International (data center)
- Two masked central readers interpreted CUS during two 2-day reading sessions
- Central reader form collected detailed hemisphere-specific radiologic observations and diagnostic data
 - Hintz SR, et. al. *J Pediatr* 2007;150:592



Methods: Analysis

- Reliability analysis by kappa statistic
 - $\text{Kappa} = \frac{\% \text{ observed agreement} - \% \text{ expected agreement}}{100\% - \% \text{ expected agreement}}$
 - ≥ 0.75 considered “substantial” to “excellent” agreement
- Accuracy analysis by sensitivity and specificity
 - Each central reader as “gold standard” against which local reader was compared

Fleiss JL, Statistical Methods, 1981; Landis JR, Biometrics, 1977



Results: Cohort and CUS scans

- **572 infants with early and late CUS**
- Early CUS obtained at $8_{\pm}4$ days of age
 - Median: 7 days
- Late CUS obtained at $37_{\pm}2$ weeks PMA
 - Median: 37 weeks PMA



Baseline Characteristics

N	572
BW, mean (SD)	848 (190) grams
EGA, mean (SD)	25.9 (1) weeks
Multiple gestation	23%
Male	56%
Race	
Non-Hispanic Black	30%
Non-Hispanic White	43%
Male	56%
Antenatal steroids	95%
Cesarean section	69%
Apgar score <3 at 5 minutes	3%
Maternal education < HS	21%



Central reader findings: **Early CUS**

	Central Reader 1	Central reader 2
EARLY CUS findings		
	N=572	N=572
Normal	72.0%	71.7%
Normal or choroid plexus bleed/cyst only	74.6%	72.6%
Any GMH or IVH	19.6%	20.8%
Grade 1 or 2	14.2%	12.2%
Grade 3 or 4	6.8%	9.6%
Any ventricular enlargement	8.8%	9.4%
Moderate-severe ventricular enlargement	4.6%	4.6%
PVL (echodense or echolucent)	1.1%	0.5%
Cerebellar/posterior fossa lesion	1.6%	1.2%



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Progression of Findings

- Of those with **normal early CUS**
 - ~80% remained **normal** on late CUS
 - 81% central reader 1; 82% central reader 2
 - Only 1% had moderate-severe ventriculomegaly on late CUS
- Of those with **grade 3 or 4** on early CUS
 - ~25% progressed to porencephalic cyst on late CUS
 - 26% central reader 1; 25% central reader 2



Central Reader Reliability: Early CUS

	Kappa	95% CI	PPA
EARLY CUS			
Normal vs. abnormal	0.76	(0.70, 0.82)	93%
Any GMH or IVH	0.79	(0.73, 0.85)	81%
Grade 1 or 2	0.52	(0.43, 0.61)	56%
Grade 3 or 4	0.77	(0.67, 0.87)	74%
Grade 3 or 4 or cPVL	0.75	(0.65, 0.85)	73%
Moderate-severe ventricular enlargement	0.84	(0.73, 0.95)	85%
PVL (echodense or echolucent)	0.22	(-0.15, 0.58)	22%



Central Reader Reliability: Late CUS

	Kappa	95% CI	PPA
LATE CUS			
Normal vs. abnormal	0.66	(0.59, 0.73)	90%
ANY ventricular enlargement	0.88	(0.83, 0.94)	89%
Moderate-severe ventricular enlargement	0.90	(0.84, 0.97)	91%
Echolucent PVL (cPVL)	0.45	(0.19, 0.71)	46%
Porencephalic cyst (P-cyst)	0.76	(0.58, 0.93)	76%
cPVL or P-cyst or any ventriculomegaly or shunt	0.84	(0.79, 0.90)	86%
cPVL or P-cyst or moderate to severe ventriculomegaly or shunt	0.88	(0.82, 0.94)	89%



Accuracy of Local Interpretation Early CUS

	Central Reader 1		Central Reader 2	
	Sensitivity	Specificity	Sensitivity	Specificity
Normal	90.3%	78.1%	88.0%	71.6%
Any GMH or IVH	92.0%	92.2%	80.7%	90.5%
Grade 1 or 2	90.1%	86.6%	71.4%	82.3%
Grade 3 or 4	89.7%	96.1%	72.7%	96.9%
Any ventricular enlargement	72.5%	97.1%	51.4%	97.2%
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NICHD Neonatal Research Network

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NICHD



NICHD Neonatal Research Network Centers (1996-2006)

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- Research Triangle Institute
- Stanford University
- University of Alabama – Birmingham
- University of California – San Diego
- University of Cincinnati
- University of Miami
- University of New Mexico
- University of Rochester
- University of Tennessee – Memphis
- University of Texas, Southwestern – Dallas
- University of Texas – Houston
- Wake Forest University
- Wayne State University
- Yale University



NICHD



NICHD Neonatal Research Network Centers (2006-2011)

- Brown University
- Case Western Reserve University
- Duke University
- Emory University
- Indiana University
- Research Triangle Institute
- Stanford University
- Tufts Medical Center
- University of Cincinnati
- University of Alabama – Birmingham
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- University of Utah
- Wayne State University
- Yale University



NICHD



From: Higgins, Rosemary (NIH/NICHD) [E]
To: nfiner@ucsd.edu
Subject: FW: 2nd NEONATAL RESUSCITATION RESEARCH WORKSHOP MAY 2010
Date: Friday, April 16, 2010 3:21:01 PM
Attachments: [Colin's Letter.pdf](#)
[Information Sheet.pdf](#)
[Program.pdf](#)
Importance: High

Neil

I assume you will be using the same slides for this as are used for PAS, correct?? I just need to let the SC know that the SUPPORT Trial results will be re-presented at this meeting (along with Wade's prio presented antenatal consent talk)>

Thanks

Rose

Rosemary D. Higgins, MD

Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research Network

Pregnancy and Perinatology Branch

CDBPM, NIH

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20592

301-435-7909

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Niki Stratis [Niki.Stratis@thewomens.org.au]

Sent: Friday, April 16, 2010 3:36 AM

To: Alan Jobe; Anne Lee Solevag; Annie Janvier; Berit Holthe Munkeby; Berndt Urlesberger; Bob Lynch; Brett Manley; Britt Nakstad; Charles Christoph Roehr; Chris Beaumont; Christoph Huenseler; Claus Klingenberg; Colin Morley; Daniel Draper (for Gerald Hunt); Edgardo Szyld; Fernando Martinez (for Neil Finer); Fiona Wood; Georg Schmoelzer; Gerald Hunt; Gianluca Lista; Graeme Polglase; Hany Aly; Helene Osterholt; Helmut Hummler; Henrik Verder; Ingrid Dannevig; Jack Rabi; Jane Pillow; Jeff Perlman; Jennifer Dawson; Jessica Faenza (for Thorsten Waloschek and Bob Lynch); John Kattwinkel; Karen Kirby (for Myra Wyckoff); Karen Link (for Alan Jobe); Keith Barrington; Khalid Aziz; Lex Doyle; Linda Wright; Lou Halamek; Maria Brugada Montaner; Maria Fernanda Almeida; Marilyn Escobedo; Mario Rojas; Marta Aguar Carrascosa; Martin Leckie; Masanori Tamura; Max Vento; Max Vento; Megan Wallace; Michael O'Reilly; Mike Meyer; Myra Wyckoff; Nalini Singhal; Neil Finer; Noah Hillman; Ola Saugstad; Omar Kamlin; Stonebanks, Paula (NIH/OD) [E]; Peter Davis; Richard Martin; Robert Kopotic; Ronnaug Solberg; Higgins, Rosemary (NIH/NICHD) [E]; Ruth Guinsburg; Stuart Hooper; Suhas Kallapur; Susan Niermeyer; Thorsten Waloschek; Tina Leone; Raju, Tonse (NIH/NICHD) [E]; Wade Rich

Subject: 2nd NEONATAL RESUSCITATION RESEARCH WORKSHOP MAY 2010

Dear Colleagues

Thank you for agreeing to come to the 2nd Neonatal Resuscitation Research Workshop.

The SPR and our resuscitation meeting is fast approaching.

Attached is Colin's letter, information sheet and the long awaited final program.

Thank you to our sponsors – Fisher and Paykel Healthcare, Masimo and Draeger for making this meeting possible.

Please read everything carefully.

I do hope you have a wonderful time in Vancouver at the SPR and at the 2nd Neonatal Resuscitation Research Workshop.

Yours sincerely

Niki Stratis
Assistant to Professor/Director of Neonatal Medicine
Newborn Research
Level 7, Room 166
The Royal Women's Hospital
20 Flemington Road
Parkville Vic 3052
Australia
Phone: + 613 8345-3763
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This email transmission and any documents attached may contain confidential information. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution or use of this transmission is strictly prohibited. If you have received this transmission in error, please immediately notify the sender and destroy the original.

16th April 2010

2nd Neonatal Resuscitation Research Workshop
Granville Island Hotel, Vancouver.
May 4th (evening), 5th and 6th.

Dear friends,

The 2nd Neonatal Resuscitation Research Workshop is less than a month away so here are your final instructions – so please read carefully.

- The program is attached.
- This workshop is to hear about the latest research but also to enjoy plenty of time to for free, frank, witty informed discussion. Please do your best to be at the lunches and dinners.
- There are 20 minutes for each presentation. PLEASE NOTE this is ten minutes presentation and then 10 minutes discussion. Please stick to this and make sure your presentation will fit into 10 minutes – 10 slides.
- You will see we have a lot to get through so we must keep to time.
- Please end your presentation with thoughts about how neonatal resuscitation may be improved or future research plans.
- You are all booked into the Granville Island Hotel unless you have let Niki know that you will be staying elsewhere. This is because we want you to get to know each other to discuss mutual research, build research synergy and collaborations and plan future research.
- We will pay for your hotel and meals during this meeting. Please note you are responsible for any travel or incidental expenses.
- We do not require abstracts.
- We are not planning to publish the proceeding of the meeting for several reasons: 1) almost all the research will soon be published in peer reviewed journals. 2) if it is not about to be published you probably don't want it in the public domain. 3) the research is on such varied topics that it is difficult to pull it all together into a 3000 word cohesive article.

If this is half as good as the Hawaii meeting we will have fun, learn a lot and hopefully improve the care of the babies in the future.

See you soon in Vancouver.

Best wishes,

Colin



2nd NEONATAL RESUSCITATION RESEARCH WORKSHOP
Tuesday 4th May (evening of) to Thursday 6th May 2010

INSTRUCTION SHEET

The Granville Island Hotel
1253 Johnston Street
Vancouver, BC
Canada V6H 3R9
Telephone: (604) 683-7373
Facsimile: (604) 683-3061
www.granvilleislandhotel.com

Check In/Check Out:

Check in time is **2.00 p.m.** and checkout time is **12:00 p.m.**

Just turn up to the front desk and state your name. Partner's names have also been passed on to the hotel.

Name Badges:

Name badges will be made available via **Jennifer Dawson**. Partners will also be receiving one.

Accommodation:

If you have requested accommodation in your registration form, this has been booked and fees will be paid by us for the following nights: Night of Tuesday 4th May, Night of Wednesday 5th May, Night of Thursday 6th (if requested) May 2010.

Meals and drinks that WILL BE paid by us:

All morning, afternoon, late afternoon teas, lunches and dinners for you will be paid by us. Dinners for spouses will be paid by us.

Meals and drinks that WILL NOT be paid by us:

Breakfast is **NOT** included. This means if you would like breakfast, you will need to order and settle the payment personally.

All alcoholic and non alcoholic drinks such as soft drinks (pop) during the lunches and dinners will **NOT** be paid by us. However a bar will be made available to purchase drinks individually during these meals.

Lunches for spouses will **NOT** be paid by us.

Other items that WILL NOT be paid by us:

1. Airfares
2. Incidental expenses such as bar and room services
3. Personally ordered meals such as room service
4. Telephone and Internet charges
5. Laundry charges
6. Tips
7. Accommodation upgrades

AV Equipment:

Available AV equipment will be - a data projector, laptop computer, screen, microphones and lectern.

Program: Program is included in the e-mail message attached to this document.

How to get to the Granville Island Hotel:

From the north:

Enter downtown via Georgia Street.

Turn right on Burrard Street and head south over the Burrard Street Bridge.

Turn left on 2nd Avenue, drive three blocks and turn left on Anderson Street (at the traffic light underneath the Granville Street Bridge).

Turn left on Anderson street to enter Granville Island.

Once you enter the Island the road will automatically make you turn right onto Cartwright Street at the Kids Market.

Follow Cartwright Street to the very end as the hotel is located on the northeast tip of Granville Island where Cartwright meets Johnston Street.

The building is white with red trim and a fluorescent red sign that reads "The Granville Island Hotel."

From the Airport:

Follow the signs into Vancouver. Take the Granville Street exit from the Arthur Lang Bridge and follow Granville Street to 16th Avenue.

Turn left on 16th Avenue and take the first right on Fir Street. Follow Fir Street to 2nd Avenue.

Turn right on 2nd Avenue. Turn left on Anderson street to enter Granville Island.

Once you enter the Island the road will automatically make you turn right onto Cartwright Street at the Kids Market. Follow Cartwright Street to the very end as the hotel is located on the northeast tip of Granville Island where Cartwright meets Johnston Street.

The building is white with red trim and a fluorescent red sign that reads "The Granville Island Hotel." Taxi Fare is approximately \$25 CDN form the airport to the hotel.

From the south:

Take highway 99 - which turns into Oak Street - into Vancouver.

Turn left on 12th Avenue, turn right on Hemlock Street and follow it under (not over) the Granville Street Bridge.

At the bottom of the hill there is a stop light, turn left at the light. Get into the right hand lane and take the first right hand turn on Anderson to enter Granville Island.

Go straight through the four way stop at 2nd Avenue and Anderson. Stay in the right hand lane. At which point you will be entering Granville Island.

Once you enter the Island the road will automatically make you turn right onto Cartwright Street at the Kids Market.

Follow Cartwright Street to the very end as the hotel is located on the northeast tip of Granville Island where Cartwright meets Johnston Street. The building is white with red trim and a fluorescent red sign that reads "The Granville Island Hotel."

From the east:

Enter Vancouver via Highway 1, and take the Grandview Highway exit. Grandview turns into 12th Avenue.

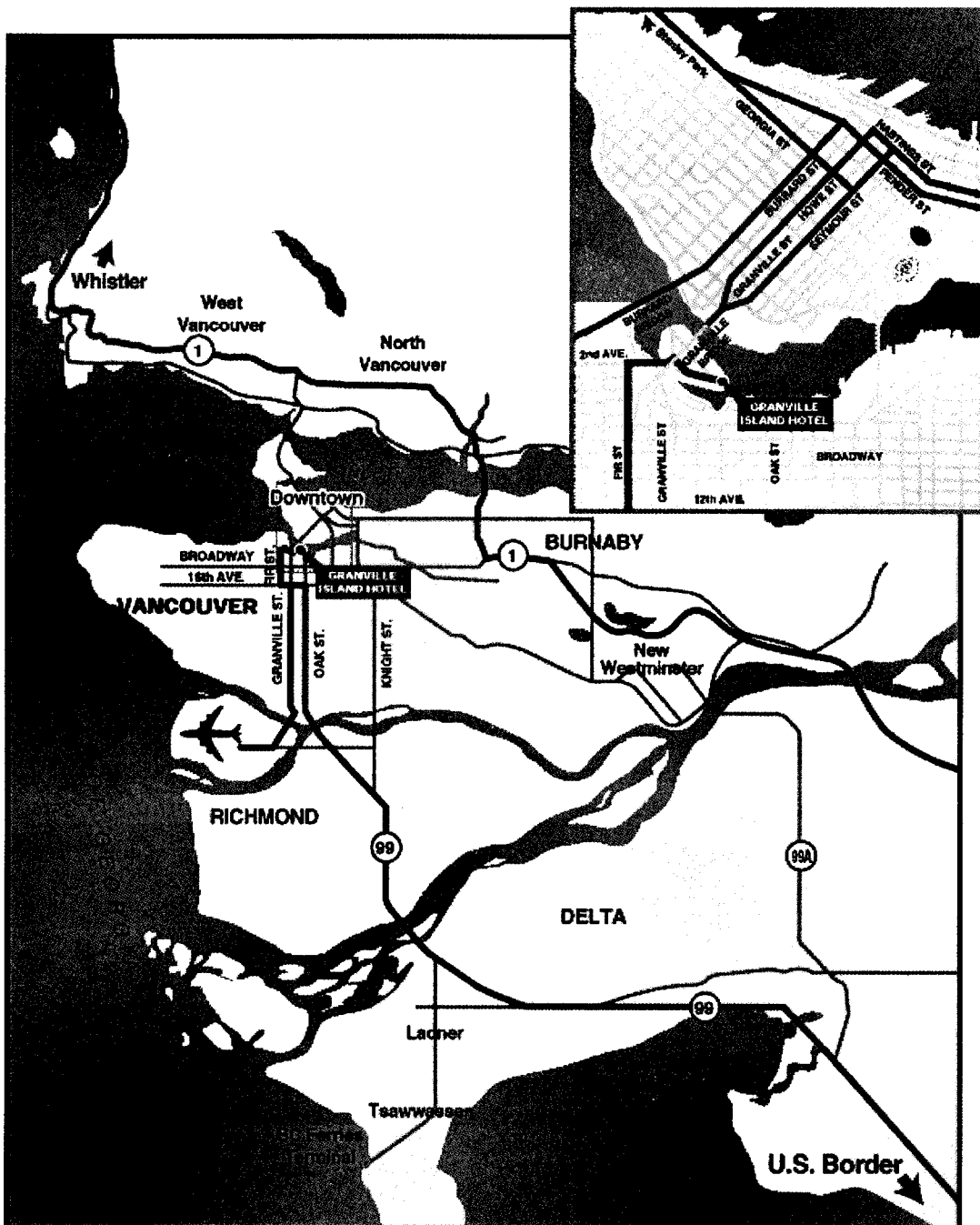
Follow 12th to Fir Street, turn right, then turn right again at 2nd Avenue.

The next street is Anderson Street (underneath the Granville Street Bridge). Turn left on Anderson to enter Granville Island.

Once you enter the Island the road will automatically make you turn right onto Cartwright Street at the Kids Market.

Follow Cartwright Street to the very end as the hotel is located on the northeast tip of Granville Island where Cartwright meets Johnston Street.

The building is white with red trim and a fluorescent red sign that reads "The Granville Island Hotel."



9:00 – 9:30 am
Jane Hill
Hello, clamping established

9:30 – 9:40 am
Masahito Tamura
Different way of clamping

9:40 – 10:00 am
MORNING TEA – Quarter Deck and Bridge

10:00 – 10:20 am (Chairperson: Susan Niermeyer)
Susan Niermeyer
Field testing of global educational program for neonatal resuscitation

10:20 – 10:40 am
Ruth Guinsburg
Deaths up to 6 days after birth associated with intrauterine hypoxia or asphyxia in Brazil: a 2005-2007 national study.

10:40 – 11:00 am
Rosemary Higgins
Challenges and opportunities for research in the Neonatal Research Network.

11:00 – 11:20 am
Maria Fernanda Branc de Almeida
Hypothermia in preterm newborn infants <34 weeks born in the Brazilian Neonatal Network: a prospective study from delivery room to NICU admission.

11:20 – 11:40 am
Brett Manley
Clinical assessment of newborns remaining in the delivery room is a poor indicator of survival

11:40 – 12:30 pm
LUNCH – Dockside Restaurant

12:30 – 12:50 pm (Chairperson: Myra Wyckoff)
Stuart Hooper
Cardiovascular transition at birth and the potential benefit of delayed cord clamping

12:50 – 1:10 pm
Khalid Aziz
Practical application of delayed cord clamping

1:10 – 1:30 pm
Marilyn Escobedo
Echocardiographic assessment of transitional circulation

1:30 – 1:50 pm
Michael Meyer
SVC flow and cord clamping.

1:50 – 2:10 pm
AFTERNOON TEA – Quarter Deck and Bridge

2:10 – 2:30 pm (Chairperson: Susan Niermeyer)
Lou Halamek
Value of simulation and debriefing in neonatal resuscitation.

2:30 – 2:50 pm
Wade Rich
The problems of antenatal consent in delivery room RCTs.

2:50 – 3:10 pm
Myra Wyckoff
Impact of delivery room CPR on the outcome of preterm infants.

3:10 – 3:30 pm
Anne Lee Solevag
What is the optimal compression ventilation ratio?

3:30 – 3:50 pm
Late Afternoon Tea – Quarter Deck and Bridge

3:50 – 4:10 pm
Ingrid Dannevig
Can the number of newborns receiving cardiac compressions be reduced?

4:10 – 4:30
Colin Morley
Personal views of 40 years of neonatal resuscitation

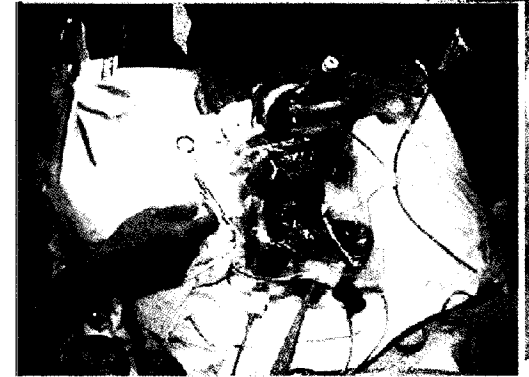
4:30 – 4:50 pm
Alan Jobe
Send us away wiser

7:30 pm
DINNER – Dockside Restaurant

2nd Neonatal Resuscitation

Research Workshop

4th - 6th May 2011



*Quarter Deck and
Bridge Rooms*

*The Granville Island Hotel
1253 Johnston Street
Vancouver, BC*

Canada

Fisher & Paykel  **MASIMO**
HEALTHCARE
Dräger



Tuesday 4th May

7.30 pm Welcome Dinner
Dockside Restaurant
The Granville Island Hotel

Wednesday 5th May

8.00 – 8.10 am (Chairperson: Richard Martin)
Colin Morley

Welcome and why are we here?

8.10 – 8.30 am

Ola Saugstad

Metabolomic analyses of plasma. New insights into asphyxia and resuscitation in pigs.

8.30 – 8.50 am

Max Vento

Oxidative stress.

8.50 – 9.10 am

Hany Aly

Oxygen-toxicity from mother to baby.

9.10 – 9.30 am

Neil Finer

SUPPORT trial report of oxygen arm.

9.30 – 9.50 am

Annie Janvier

Clinical ethics orientated resuscitation research.

9.50 – 10.10 am

MORNING TEA – Quarter Deck and Bridge

10.10 – 10.30 am (Chairperson: Keith Barrington)

Jennifer Dawson

SpO₂ and heart rate centiles in the delivery room – how should they be used?

10.30 – 10.50 am

Robert Kopotic

Comparison of cerebral and pulse oximetry.

10.50 – 11.10 am

Helmut Hummel

Brain tissue oxygenation during resuscitation

11.10 – 11.30 am

Berndt Uriesberger

Regional oxygen saturation of the brain differs from peripheral tissue during transition of the newborn.

11.30 – 11.50 am

Richard Martin

Intermittent hypoxic episodes as an oxidant stress.

11.50 am – 12.10 pm

Wade Rich, Neil Finer or Max Vento

The PreSox trial.

12.10 pm

LUNCH – Dockside Restaurant

1.00 – 1.20 pm (Chairperson: Jeff Perlman)

Stuart Hooper

Facilitating lung aeration at birth.

1.20 – 1.40 pm

Claus Klingenberg

Devices for delivering sustained inflations.

1.40 – 2.00 pm

Edgardo Szyld

Study comparing a T piece vs a self inflating bag.

2.00 – 2.20 pm

Megan Wallace

Effect of a sustained inflation on markers of lung injury.

2.20 – 2.40 pm

Gianluca Lista

Sustained lung inflation in the delivery room: personal experience.

2.40 – 3.00 pm

Afternoon Tea – Quarter Deck and Bridge

3.00 – 3.20 pm (Chairperson: Peter Davis)

Tina Leone

End tidal CO₂ and ventilation in the delivery room.

3.20 – 3.40 pm

Christoph Huenseler

Monitoring of respiratory function after birth: use of a Respiratory Function Monitor

3.40 – 4.00 pm

John Kattwinkel

Effect of changing compliance on tidal volume delivery.

4.00 – 4.20 pm

Christoph Huenseler

Surfactant delivery through a thin catheter.

4.20 – 4.40 pm

Mario Rojas

Very early surfactant and nCPAP in the delivery room.

4.40 – 5.00 pm

Late Afternoon Tea – Quarter Deck and Bridge

5.00 – 5.20 pm

Neil Finer

The SUPPORT study – CPAP arm.

5.20 – 5.40 pm

Henrik Verder

Prediction (at birth) of RDS and which babies should receive surfactant.

5.40 – 6.00 pm

Thorsten Waloscheck

The Baby First initiative.

7.30 pm

Dinner – Dockside Restaurant

Thursday 6th May

8.00 – 8.20 am (Chairperson: Alan Jobe)

Graeme Polglaze

Effect of inflammation and ventilation on cerebral hemodynamics and injury.

8.20 – 8.40 am

Noah Hillman

Inflammatory progression after stretch injury of the fetal airway.

8.40 – 9.00 am

Suresh Kulkarni

Modulation of inflammation – implications for resuscitation

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Bell, Edward"
Cc: "Finer, Neil"; "Wally Carlo"
Subject: RE: SUPPORT presentations
Date: Tuesday, April 13, 2010 9:57:00 AM

Ed

This only applies to PRIOR PUBLICATION. Further, we are NOT ALLOWED to state that the papers are under review or accepted by NEJM as per the NEJM embargo policies.

Thanks
Rose

From: Bell, Edward [mailto:edward-bell@uiowa.edu]
Sent: Tuesday, April 13, 2010 9:44 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Finer, Neil; Wally Carlo
Subject: SUPPORT presentations

Rose,

Should Neil and Wally notify PAS that the papers have been accepted in NEJM? Maybe they have already done to.

See below from: http://www.pas-meeting.org/2010Vancouver/Abstracts/default.asp#Technical_Support

Prior Publication

Should not be submitted to PAS; if research has been published in manuscript form, it can be submitted, but the PAS office must be notified if it has been submitted, but not yet accepted OR will be published after the meeting.

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Monday, April 12, 2010 9:45 AM
To: Peter Brocklehurst
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.
Subject: RE: SUPPORT

Hello Peter

The abstracts are generally correct. The data for the final manuscripts was somewhat different with respect to the significant differences - more so for the CPAP_Surf than for the SPO2 Paper.

The final manuscript for the SPO2 paper is not yet accepted in final form.

we did share the results with the DSMCs of all trials at the completion of the trials For now, assume that the results in the sPO2 manuscript are the correct ones.

I am waiting for a publication date of the manuscripts.

Hope to see you at PAS where we will present in more detail Be well Neil

-----Original Message-----

From: Peter Brocklehurst [mailto:Peter.Brocklehurst@npeu.ox.ac.uk]
Sent: Monday, April 12, 2010 1:06 AM
To: Finer, Neil
Subject: SUPPORT

Dear Neil

As you might imagine the SUPPORT abstract on the PAS website has caused quite a stir amongst the remaining trials teams! We in the UK are in the process of discussing your results with our Trial Steering Committee and Data Monitoring Committee, but I wondered if you could let me know whether the results in the abstract (particularly in relation to death) are the same as those that are going to be presented at PAS or in the current draft of the paper? Abstracts are sometimes submitted well before the conference and it appears that the denominators in the table are different from the number of babies randomised suggesting that outcomes were not known for all babies - although this may be my error.

We still need to pull together our TSC and DMC to discuss the results which you present at PAS, but the urgency with which we do this may be modified by knowing whether the abstract contains the final results or not! Any information you are able to provide me with, would be really helpful.

Many thanks

Best wishes

Peter

Peter Brocklehurst
Professor of Perinatal Epidemiology
Director
National Perinatal Epidemiology Unit
University of Oxford
Old Road Campus

Headington
Oxford
OX3 7LF
Tel: 01865 289719
Fax: 01865 289720

Best wishes

Peter

Peter Brocklehurst
Professor of Perinatal Epidemiology
Director
National Perinatal Epidemiology Unit
University of Oxford
Old Road Campus
Headington
Oxford
OX3 7LF
Tel: 01865 289719
Fax: 01865 289720

From: Shankaran, Seetha
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally
Cc: Shankaran, Seetha
Subject: RE: Confidential PAS Presentation Finer SUPPORT 2010-04-06.ppt
Date: Saturday, April 10, 2010 3:37:51 PM

Wally

Great slides, sorry for not getting back earlier--just minor comments.

Slide 16 maybe take off ";".

If time is of essence, you could exclude Slide 16.

For Slide 17 can you * BPD--appears significant

I think slide 29 is very interesting data---and should be explored for another paper---

Thanks

Seetha

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Tuesday, April 06, 2010 12:44 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; 'Abhik Das'; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; cotte010@mc.duke.edu; 'Dennis Wallace'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; 'Kristi Watterberg'; Kurt Schibler [kurt.schibler@cchmc.org]; 'Matthew Bizzarro'; 'Michelle Walsh'; 'MIckey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; 'Roger Faix'; 'Ronald GOLdberg'; Shankaran, Seetha; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; VanMeurs, Krisa
Cc: 'Finer, Neil'; Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Cunningham, Meg'; 'Huitema, Carolyn Petrie'
Subject: RE: Confidential PAS Presentation Finer SUPPORT 2010-04-06.ppt

Here is Wally's presentation for PAS. Please send comments directly to Wally

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, April 06, 2010 12:19 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Finer, Neil'; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: Confidential PAS Presentation Finer SUPPORT 2010-04-06.ppt
Importance: High

Hi,

Attached is Neil's presentation for PAS. If you have any comments, please send them to Neil.

Please keep this information confidential. **We are not to discuss the fact that the papers have been reviewed or accepted**

by NEJM. PI's - please insure that all of your staff with the confidential knowledge regarding the SUPPORT papers are aware of the NEJM rules!!

In addition, since the papers are not yet published in NEJM, we need to respect their embargo policy. This means that we are requested to follow the guidelines at <http://authors.nejm.org/Help/Embargo.asp>.

Specifically, the guidelines state:

- Please do not discuss the fact that the research has been submitted or accepted for publication in the *New England Journal of Medicine*.
- Please do not distribute any copies of the manuscript, tables, or figures. (It is acceptable to use the materials in a presentation, but they should not be distributed.)

Meeting organizers may promote an author's presentation in a press release, plan a press conference, publish the abstract in a meeting proceedings, and/or post the presentation on their Web site. We ask that authors, their institutions, and other organizations sponsoring the research not do any further promotion of the presentation

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Bock, Robert (NIH/NICHD) [E]
Subject: FW: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783
Date: Friday, April 09, 2010 9:11:00 AM

From: Buckley, Karen [mailto:kbuckley@nejm.org]
Sent: Monday, April 05, 2010 2:20 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Solomon, Caren, M.D.
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Dear Dr. Higgins,

To answer your question, presenting at the meetings you have described will not preclude publication. You are not restricted as far as the information you present, and are correct in your understanding that you should not mention NEJM as part of those presentations. If pressed, you might say that your paper is under consideration at a peer-reviewed journal. You may respond to media questions about your presentation. There are guidelines outlined at <http://authors.nejm.org/Help/Embargo.asp> (see bottom half of page), but if you have further questions, please let me know.

If publication is coordinated with presentation, the rules change mainly in that you can acknowledge publication in NEJM. We can go over that in more detail if/when the situation arises.

Best,

Karen

Karen Pedersen Buckley
Manager, Media Relations
The New England Journal of Medicine
Media Relations 781-434-7847
Private line 781-434-7579
kbuckley@nejm.org

From: Solomon, Caren, M.D.
Sent: Monday, April 05, 2010 2:10 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'
Cc: Buckley, Karen
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Rose,

I am forwarding your inquiry to Karen Buckley, who handles media relations questions..

But a question for you.. In some cases, we post articles early on line to concord with academic meetings... This is not always possible (depends on how tight the timeline, number of manuscripts already being expedited etc)

but is this something we should be considering as a possibility? And if yes, would you be thinking of this at time of ATS mtg? (ie might earlier publication, if even conceivable, pose a problem for ATS presentations ?)

Let me know your thoughts on this and I will raise with my colleagues.

Caren

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 05, 2010 1:59 PM
To: Solomon, Caren, M.D.
Cc: 'Finer, Neil'; wacarlo@uab.edu
Subject: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Caren

We would like to review the embargo policy that NEJM has for accepted manuscripts as we have two sets of upcoming presentations for the NICHD NRN SUPPORT TRIAL. Neil will present the CPAP SURFACTANT study and Wally will present the Saturation arms of the study at the Pediatric Academic Society meetings in Vancouver, BC on May 1 and 2. Both Neil and Wally will again present the trial results at the American Thoracic Society meeting on May 16 in New Orleans. It is our understanding from the Embargo guidelines that presentation at medical meetings is permissible, but we are not allowed to state that the manuscripts are accepted for publication in NEJM and we should refrain from discussing study results with the media at these meetings.

Do we have this correct??

Thanks for your help.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

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From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: P.S.
Date: Friday, April 09, 2010 9:06:51 AM

Was there enough NHLBI support to merit my offering them a joint NICHD/NHLBI release?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 09, 2010 9:06 AM
To: Bock, Robert (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]
Subject: RE: SUPPORT news release 6cys

Ok

Can you also send it to Carol Blaisdell and Dorothy Gale in the Lung Division as they have been instrumental in the support we received from NHLBI?

Thanks
Rose

From: Bock, Robert (NIH/NICHD) [E]
Sent: Friday, April 09, 2010 9:04 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]
Subject: RE: SUPPORT news release 6cys

Thanks. Before we send the release out over our lists or post it on our Web site, we'll strip out the urls and include only the hyperlinks in the text. For some reason that I don't know, NIH OLIB has us include urls after each hyperlink in the clearance copy.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 09, 2010 8:32 AM
To: Bock, Robert (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]
Subject: SUPPORT news release 6cys

Bob - see my comments to Cathy's comments - I agree with all her suggestions. Up to you regarding the web links - this may be good for lay folks/parents who might read this

Thanks
Rose

From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [Spong, Catherine \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT news release 6cys
Date: Friday, April 09, 2010 9:06:11 AM

Sure. I'll cc them when I send it to Susan and Diane in the NHLBI press office.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 09, 2010 9:06 AM
To: Bock, Robert (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]
Subject: RE: SUPPORT news release 6cys

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From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, April 09, 2010 8:32 AM
To: Bock, Robert (NIH/NICHD) [E]
Cc: Spong, Catherine (NIH/NICHD) [E]
Subject: SUPPORT news release 6cys

Bob - see my comments to Cathy's comments - I agree with all her suggestions. Up to you regarding the web links - this may be good for lay folks/parents who might read this

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Phelps, Dale"; "Laroja, Nirupama"; "Michael O' Shea"; "Duara, Shahnaz"
Cc: "Finer, Neil"; "Wally Carlo, M.D."; "Das, Abhik"
Subject: SUPPORT PAS AND ATS presentations
Date: Wednesday, April 07, 2010 11:47:00 AM
Importance: High

Hi,

The SUPPORT abstracts will be presented in platforms at PAS and at a special NHLBI lunch session at ATS on May 16. We do not as of today have a publication date from NEJM.

We are not to discuss the fact that the papers have been reviewed or accepted by NEJM. PI's - please insure that all of your staff with the confidential knowledge regarding the SUPPORT papers are aware of the NEJM rules!!

In addition, since the papers are not yet published in NEJM, we need to respect their embargo policy. This means that we are requested to follow the guidelines at <http://authors.nejm.org/Help/Embargo.asp>.

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Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Bock, Robert \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT news release 4
Date: Wednesday, April 07, 2010 11:37:10 AM

So was it part of the study, or did it come after?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, April 07, 2010 11:37 AM
To: Bock, Robert (NIH/NICHD) [E]
Subject: RE: SUPPORT news release 4

The Nasal canula came after the children received their initial treatment (i.e. in the "getting better" phase of their illness and NICU course)

From: Bock, Robert (NIH/NICHD) [E]
Sent: Wednesday, April 07, 2010 11:36 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT news release 4

Were there enough kids on the nasal canula in this study to mention it in the release? Didn't the study just talk about the comparison between the ventilator/surfactant group, and the CPAP group?

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, April 07, 2010 11:33 AM
To: Bock, Robert (NIH/NICHD) [E]
Subject: SUPPORT news release 4

I shortened the Guttmacher quote - and yes, the canula is what the older folks with COPD/emphysema use. Let me know when this goes over to NHLBI (they may want to insert a quote also)

Rose

From: Roger Faix
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Confidential PAS PResentation Finer SUPPORT 2010-04-06.ppt
Date: Tuesday, April 06, 2010 8:24:58 PM

Again, many thanks!

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Tuesday, April 06, 2010 10:44 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; 'Abhik Das'; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Bradley Yoder; 'Brenda Poindexter'; 'Carlo Waldemar (E-mail)'; cotte010@mc.duke.edu; 'Dennis Wallace'; 'Ed Bell'; 'Ed Donovan'; 'Ehrenkranz Richard (E-mail)'; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; 'Kristi Watterberg'; Kurt Schibler [kurt.schibler@cchmc.org]; 'Matthew Bizzarro'; 'Michelle Walsh'; 'Mickey Caplan'; 'Oh William (E-mail)'; 'Pablo Sanchez'; 'Poole Kenneth (E-mail)'; Roger Faix; 'Ronald GOLDBERG'; 'Seetha Shankaran'; 'Stevenson David (E-mail)'; 'Stoll Barbara (E-mail)'; 'Tyson Jon (E-mail)'; VanMeurs, Krisa
Cc: 'Finer, Neil'; Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Cunningham, Meg'; 'Huitema, Carolyn Petrie'
Subject: RE: Confidential PAS PResentation Finer SUPPORT 2010-04-06.ppt

Here is Wally's presentation for PAS. Please send comments directly to Wally

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, April 06, 2010 12:19 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: Confidential PAS PResentation Finer SUPPORT 2010-04-06.ppt
Importance: High

Hi,

Attached is Neil's presentation for PAS. If you have any comments, please send them to Neil.

Please keep this information confidential. **We are not to discuss the fact that the papers have been reviewed or accepted by NEJM.** PI's - please insure that all of your staff with the confidential knowledge regarding the SUPPORT papers are aware of the NEJM rules!!

In addition, since the papers are not yet published in NEJM, we need to respect their embargo policy. This means that we are requested to follow the guidelines at

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From: Roger Faix
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Confidential PAS PReSentation Finer SUPPORT 2010-04-06.ppt
Date: Tuesday, April 06, 2010 8:23:19 PM

Thanks, Rose! I'll review and get back to Neil as needed. I will certainly respect the embargo rules (many thanks for the link),

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Tuesday, April 06, 2010 10:19 AM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Bradley Yoder; Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: Confidential PAS PReSentation Finer SUPPORT 2010-04-06.ppt

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From: Archer, Stephanie (NIH/NICHD) [E]
To: Neil Finer (nfiner@ucsd.edu)
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Confidential PAS PResentation Finer SUPPORT 2010-04-06.ppt
Date: Tuesday, April 06, 2010 3:00:55 PM

Hi Neil,

Here are my comments on your slides:

General:

- Change the Page Setup from "35mm slides" to "On-screen Show", so make sure that the full slide shows up when projected. This will change the page size, so you will have to adjust some slides to fit everything back onto them
- In general too many words for people across the room to read easily.

Title slide: pictures overlap words, the bottom stripe is distracting (need to keep the logos, but take the blue out of the stripe).

Slide 5: words off the bottom of the slide

Slides 18, 19, and 21: add lines to the table to make it easier to follow across the rows/columns.

Slide 19: Lots of blank space on the table header.

Slide 23: words off the bottom of the slide

Slides 28 and 29: font too small to see across the room

Stephanie Wilson Archer
The Eunice Kennedy Shriver
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Pregnancy & Perinatology Branch
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Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tuesday, April 06, 2010 12:19 PM
To: (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Finer, Neil; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: Confidential PAS PResentation Finer SUPPORT 2010-04-06.ppt
Importance: High

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From: [Susan Hintz](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: ATS?
Date: Monday, April 05, 2010 8:28:15 PM

Hi Rose

I have on my calendar a cryptic little reminder that says "SUPPORT presentation at ATS" on May 16. Is there something I should be preparing for that? Or maybe I just put it on my calendar to be there to support SUPPORT.

Thanks

Susan

Sent from my iPhone

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Wally Carlo, M.D."; "Finer, Neil"
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783
Date: Monday, April 05, 2010 2:46:00 PM

I had that in the email below

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Monday, April 05, 2010 2:41 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

She may not be aware of the PAS meeting three weeks earlier but the timing may be too tight for PAS.

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 05, 2010 1:35 PM
To: 'Solomon, Caren, M.D.'
Cc: Buckley, Karen; 'Finer, Neil'; Wally Carlo, M.D.
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Caren

It would be great if we could coordinate the publication with the ATS presentation (May 16). The ATS presentation is at an NHLBI noon session:

L4 OUTCOMES FROM THE NHLBI-NICHD SUPPORT TRIAL: THE SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY TRIAL IN EXTREMELY LOW BIRTH WEIGHT (ELBW) INFANTS

I have checked with the NHLBI folks and publication does not preclude presentation at this meeting. It would be great if publication and presentation can happen around the same time. Let us know if there is anything we can do from our end to facilitate this. Thanks for your consideration.

Rose

From: Solomon, Caren, M.D. [mailto:csolomon@nejm.org]
Sent: Monday, April 05, 2010 2:10 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Buckley, Karen
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Rose,

I am forwarding your inquiry to Karen Buckley, who handles media relations questions..
But a question for you.. In some cases, we post articles early on line to concord with academic meetings... This is not always possible (depends on how tight the timeline, number of manuscripts already being expedited etc)
but is this something we should be considering as a possibility? And if yes, would you be thinking of this at time of ATS mtg? (ie might earlier publication, if even conceivable, pose a problem for ATS presentations ?)
Let me know your thoughts on this and I will raise with my colleagues.
Caren

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, April 05, 2010 1:59 PM
To: Solomon, Caren, M.D.
Cc: 'Finer, Neil'; wacarlo@uab.edu
Subject: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

Caren

We would like to review the embargo policy that NEJM has for accepted manuscripts as we have two sets of upcoming presentations for the NICHD NRN SUPPORT TRIAL. Neil will present the CPAP SURFACTANT study and Wally will present the Saturation arms of the study at the Pediatric Academic Society meetings in Vancouver, BC on May 1 and 2. Both Neil and Wally will again present the trial results at the American Thoracic Society meeting on May 16 in New Orleans. It is our understanding from the Embargo guidelines that presentation at medical meetings is permissible, but we are not allowed to state that the manuscripts are accepted for publication in NEJM and we should refrain from discussing study results with the media at these meetings.

Do we have this correct??

Thanks for your help.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: ["Wally Carlo, M.D."](#)
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783
Date: Monday, April 05, 2010 2:01:00 PM

Neil had called me about this

Rose

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Monday, April 05, 2010 2:01 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: upcoming presentations of the NICHD NRN SUPPORT Trial 09-11781 and 09-11783

THANKS! Very well worded.

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
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Phone: 205 934 4680
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From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
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Do we have this correct??

Thanks for your help.

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From: [Colin Morley](#)
To: [Marta Aguar](#); [Maria Fernanda Branco De Almeida](#); [Hany Aly](#); [Khalid Aziz](#); [Keith Barrington](#); [Maria Brugada](#); [Jon Church](#); [Ingrid Dannevig](#); [Peter Davis](#); [Jennifer Dawson](#); [Lex Doyle](#); [Marilyn B. \(HSC\) Escobedo](#); [Neil Finer](#); [Ruth Guinsburg](#); [Lou Halamek](#); [Ruth Morley](#); [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#); [Noah Hillman](#); [ronnaug.solberg@medisin.uio.no](#); [Stuart Hooper](#); [christoph@uni-koeln.de](#); [Helmut Hummler](#); [ghunt@masimo.com](#); [Annie Janvier](#); [Alan Jobe](#); [Suhas Kallapur](#); [Omar Kamlin](#); [John Kattwinkel](#); [William Keenan](#); [Claus Klingenberg](#); [Bob Kopotic](#); [Martin Leckie](#); [Tina Leone](#); [g.lista@icp.mi.it](#); [Bob Lynch](#); [Brett Manley](#); [Richard Martin](#); [Michael Meyer \(CMDHB\)](#); [Berit Munkaby](#); [Britt Nakstad](#); [Susan Neirmeyer](#); [Michael O'Reilly](#); [Jeffrey Perlman](#); [Jane Pillow](#); [Graeme Polglaze](#); [Jack Rabi](#); [Raju, Tonse \(NIH/NICHD\) \[E\]](#); [Wade Rich](#); [Charles Christoph Roehr](#); [Mario Rojas](#); [Ola Saugstad](#); [Georg Schmoelzer](#); [Nalini Singhal](#); [a.l.solevag@medisin.uio.no](#); [Suzuki Keiji](#); [Edgardo Eszyd](#); [Masanori Tamura](#); [berndt.urlesberger@medunigraz.at](#); [Maximo Vento](#); [Henrik Verder](#); [Megan Wallace](#); [Thorsten Waloschek](#); [Fiona Wood](#); [Wright, Linda \(NIH/NICHD\) \[C\]](#); [myra.wyckoff@utsouthwestern.edu](#)
Cc: [Niki Stratis](#)
Subject: 2nd Neonatal Resuscitation Research Workshop, Granville Island Hotel, Vancouver.
Date: Tuesday, March 30, 2010 7:45:37 AM
Attachments: [2nd Resuscitation Research Workshop Draft program.docx](#)
[ATT0001.htm](#)

Tuesday May 4 th		
7:30	Welcome dinner	? venue
Wednesday May 5 th		
8:00 to 8:10	C JM	Welcome and why are we here?
8:10 to 8:30	Ola Saugstad	Metabolomic analyses of plasma new insights into asphyxia and resuscitation in Pigs
8:30 to 8:50	Max Vento	Oxidative stress
8:50 to 9:10	Hany Aly	Oxygen toxicity from mother to baby
9:10 to 9:30	Keiji Suzuki	Oxidative stress - studies
9:30 to 9:50	Neil Finer	SUPPORT trial report of oxygen arm
9:50 to 10:10	Morning tea	
10:10 to 10:30	Jennifer Dawson	SpO ₂ and heart rate centiles in the DR – how should they be used?
10:30 to 10:50	Robert Kopotic	Comparison of cerebral and pulse oximetry
10:50 to 11:10	Helmut Hummler	Brain tissue oxygenation during resuscitation
11:10 to 11:30	Berndt Urlresberger	Regional oxygen saturation of the brain differs from peripheral tissue during transition of the newborn
11:30 to 11:50	Richard Martin	Intermittent hypoxic episodes as an oxidant stress
11:50 to 12:10	Rich or Finer or Vento	The PreSox trial
12:10 to 1:00	Lunch	
1:00 to 1:20	Stuart Hooper	Facilitating lung aeration at birth
1:20 to 1:40	Claus Klingenberg,	Devices for delivering sustained inflations
1:40 to 2:00	Edgardo Szyld	Study comparing a T piece vs. a self inflating bag
2:00 to 2:20	Megan Wallace	Effect of a sustained inflation on markers of lung injury
2:20 to 2:40	Gianluca Lista	Sustained lung inflation in the delivery room: personal experience
2:40 to 3:00	Afternoon tea	
3:00 to 3:20	Tina Leoni	End tidal CO ₂ and ventilation in the DR
3:20 to 3:40	Georg Schmölder	Monitoring of respiratory function after birth, use of a Respiratory Function Monitor
3:40 to 4:00	John Kattwinkel	Effect of changing compliance on tidal volume delivery
4:00 to 4:20	Christoph Huenseler,	Surfactant delivery through a thin catheter
4:20 to 4:40	Mario Rojas	Very early surfactant and nCPAP in the delivery room
4:40 to 5:00	Late afternoon tea	
5:00 to 5:20	Neil Finer	The SUPPORT study – CPAP arm
5:40 to 6:00	Henrik Verder	Prediction (at birth) of RDS and which babies should receive surfactant
7:30	Dinner? venue	
Thursday May 6 th		
8:00 to 8:20	Graeme Polglaze	Effect of inflammation and ventilation on cerebral hemodynamics and injury
8:20 to 8:40	Noah Hillman	Inflammatory progression after stretch injury of the fetal airway.
8:40 to 9:00	Suhas Kallapur	Modulation of inflammation - implications for resuscitation injury
9:00 to 9:20	Jane Pillow	Heliox during establishment of ventilation
9:20 to 9:40	Masanori Tamura	Different ways of tracheal suction to prevent MAS
9:40 to 10:00	Morning tea	
10:00 to 10:20	Susan Neirmeyer	Field testing of global educational program for neonatal resuscitation

10:20 to 10:40	Ruth Guinsburg	Deaths up to 6 days after birth associated with intrauterine hypoxia or asphyxia in Brazil: a 2005-2007 national study
10:40 to 11:00	Rosemary Higgins	Challenges and opportunities for research in the Neonatal Research Network
11:00 to 11:20	Maria Fernanda Branc de Almeida	Hypothermia in Preterm Newborn Infants < 34 weeks born in the Brazilian Neonatal Network: a prospective study from delivery room to NICU admission
11:20 to 11:40	Lou Halamek	Value of simulation and debriefing in neonatal resuscitation
11:40 to 12:30	Lunch	
12:30 to 12:50	Stuart Hooper	Cardiovascular transition at birth and the potential benefit of delayed cord clamping
12:50 to 1:10	Khalid Aziz	Practical application of delayed cord clamping
1:10 to 1:30	Marilyn Escobedo	Echocardiographic studies in transitional circulation
1:30 to 1:50	Michael Meyer	SVC flow and cord clamping
1:50 to 2:10	Afternoon tea	
2:10 to 2:30	Brett Manley	Clinical assessment of extremely premature infants in the delivery room is a poor predictor of survival"
2:30 to 2:50	Annie Janvier	Clinical ethics orientated resuscitation research
2:50 to 3:10	Wade Rich	The problems of antenatal consent in DR RCTs
3:10 to 3:30	Myra Wyckoff	Impact of Delivery Room CPR on the outcome of preterm infants
3:30 to 3:50	Anne Lee Solevag	What is the optimal compression ventilation ratio?
3:50 to 4:10	Late afternoon tea	
4:10 to 4:30	Ingrid Dannevig	Can the number of newborns receiving cardiac compressions be reduced?
4:30 to 4:50	Masanori Tamura	Different ways of tracheal suction to prevent MAS
4:50 to 5:10	Alan Jobe	Send us away wiser
7:30	Dinner ? venue	

Every one needs a take away message about future of resuscitation or research

Dear friends,

The 2nd Neonatal Resuscitation Research Workshop is getting closer and I have now made up a draft programme which is attached.

Please forgive me if I have not included the talk you offered. This is not intended to offend or demean your work. There are just not enough slots for everybody to present. I also wanted to cover a wide range of topics.

However, even if you are not presenting you will have lots of time to talk and be involved in the discussions. The plan is that people talk for 10 minutes and then there is 10 minutes discussion after each talk. Therefore we will have as much time for discussion as talks.

Please look at this draft program and let me, and Niki, know ASAP if there are problems - wrong title, wrong time etc.

We will be sending you details of the final program, location, dinners, accommodation, etc when Niki gets back from her holiday after Easter.

We will also send you a list of the great and good who will be at the meeting so you can see who is coming. Of course you will see a lot from the programme and the above email list.

Speakers please note that the talks will be using powerpoint. Please let me know if you need anything else.

Speakers please be concise and keep to time. I would not want the chairmen to be so rude as to stop you in the middle of your talk! Ten minutes = no more than 10 slides.

Every talk must end with a take away message for the future of neonatal resuscitation, future research directions / collaborations or improving the future care of sick babies.

We will have fun!

Best wishes and see you soon.

Colin Morley
UK mobile 07591647097
UK home phone 01223846944
23 High St, Great Shelford, Cambridge
CB22 5EH UK

PS Please can you acknowledge receipt of this email.

From: Susan Hintz
To: Newman, Jamie
Cc: Higgins, Rosemary (NIH/NICHD) [E]; vohr
Subject: Re: Please confirm: availability to provide update for NRN FU PI Mtg at PAS
Date: Friday, March 26, 2010 2:53:07 PM

Hi Jamie

I can't open the attachment from where I am, but I am available to give a SUPPORT NEURO cohort update -i am assuming I am on the list.

Thanks

Susan

Sent from my iPhone

On Mar 26, 2010, at 11:25 AM, "Newman, Jamie" <newman@rti.org> wrote:

Dear all,

We are working on the agenda for the NRN Follow-up PI meeting at PAS which will be held on Monday, May 3 from 1-3pm (see attached draft). Several of you have already confirmed to Rose that you will be able to provide a brief update (i.e., Dr. Laptook and Dr. Blakely).

For others listed in the attached agenda, please let me know if you will be attending PAS and are able to provide an update.

Thanks, Jamie

Jamie E. Newman, PhD, MPH
Statistics and Epidemiology
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

Federal Express/UPS/DHL Shipping Address:

*Jamie Newman
RTI International
Cox 330
3040 Cornwallis Road
RTP, NC 27709 USA*

<PAS 2010 NRN Follow Up Mtg Agenda.doc>

From: Juliann DiFiore
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT Intermittent Hypoxia Protocol
Date: Friday, March 26, 2010 12:43:02 PM

Thanks.

On 3/26/2010 11:24 AM, Higgins, Rosemary (NIH/NICHD) [E] wrote:

> This will be reviewed by protocol review. We are currently polling for availability from subcommittee members.
> I will let you know once we set a review date (I asked that it be in April)>

>

> Rose

>

> -----Original Message-----

> From: Juliann DiFiore [<mailto:jmd3@case.edu>]

> Sent: Friday, March 26, 2010 11:18 AM

> To: Higgins, Rosemary (NIH/NICHD) [E]

> Cc: Michele Walsh; Julie Di Fiore

> Subject: SUPPORT Intermittent Hypoxia Protocol

>

> Rose,

>

> Attached is the updated version of the SUPPORT trial intermittent
> hypoxia protocol. I believe we have addressed the concerns discussed on
> the conference call but if there are any questions please feel free to
> call/email me.

>

> Regards,

>

> Julie

>

>

>

--

Juliann Di Fiore
Research Engineer
Rainbow Babies & Children's Hospital
Division of Neonatology, Room 3100
11100 Euclid Ave
Cleveland, OH 44106
(216) 844-1478

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: ****Important NEJM acknowledgements*****
Date: Friday, March 26, 2010 11:56:00 AM

You have it correct!!
Thanks
Rose

From: Roger Faix [mailto:Roger.Faix@hsc.utah.edu]
Sent: Friday, March 05, 2010 2:51 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Karen Osborne RN
Subject: RE: ****Important NEJM acknowledgements*****

Hi Rose!

We have no names to add or delete to the boilerplate acknowledgements, BUT would suggest the following changes to the hospital names in the Utah section of the acknowledgements:

For CarloSUPPORT Final version:
Change University Hospital to University of Utah Medical Center

For FinerSUPPORT Final version:
Change University Hospital to University of Utah Medical Center

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 7:17 AM
To: 'Finer, Neil'; 'Duara, Shahnaz'; Phelps, Dale; 'Michael O` Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Bradley Yoder; Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mlckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'
Subject: ****Important NEJM acknowledgements*****

Hi,

It was brought to our attention that at least one site has a staff member missing on the acknowledgements section of the SUPPORT papers. I spoke with Brendan Abel, editorial assistant at NEJM this morning and we will be permitted to insert additional names into the acknowledgements section. He pointed out that no changes can be made to the manuscript without the approval of the editor so the attached papers are final.

Therefore, I am requesting that each Steering Committee PI (from both cycles of the NRN

involved in the study) review the two acknowledgement sections and send me any additional person(s) that deserve to be listed by *Monday March 8*. If someone is an author on the paper, they should not appear in the boilerplate. Further, please check to insure that all of the hospitals that your site recruited from are listed and that all of your staff/hospitals are correctly spelled in the documents.

The acknowledgements begin on page 20 for the CPAP/surf paper and on page 21 for the oxygen saturation paper.

Thanks for all your help and remember to keep the manuscripts confidential as NEJM has a very strict embargo policy.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Support boilerplate authorship
Date: Friday, March 26, 2010 8:40:37 AM

The files on the n drive are up to date with the changes I've received so far. I'd like you to review it to as a second pair of eyes.

I'll be on the call.

----- Original Message -----

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Sent: Thu Mar 25 19:27:16 2010
Subject: Support boilerplate authorship

Can you finalize the two support paper authorship and boilerplate documents tomorrow morning?

Also, we have set up on on 930 call with betty, Kris and jamie for the agenda for the pas meeting that i need you to join. Kris will attend in person in Vancouver and i want you there also in case there are any glitches.

Thanks
Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 2:50:12 PM

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Roger Faix [mailto:Roger.Faix@hsc.utah.edu]
Sent: Wednesday, March 24, 2010 2:49 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

I have no corrections to suggest.

Roger

From: Archer, Stephanie (NIH/NICHD) [E] [archerst@mail.nih.gov]
Sent: Wednesday, March 24, 2010 11:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; (vineet.bhandari@yale.edu); Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Bradley Yoder; Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

As many of you have pointed out, I had some duplications between the authors and having their names in the boilerplate. I have corrected that in the attached files. Please let Rose and I know by tomorrow of any additional changes you need make.

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

Hi ALL-

Attached are the two SUPPORT paper mastheads for authorship and the boilerplates.

I request that the site PI's please look at this and tell me by Thursday, March 25 if any additional changes are warranted.

Also, Dr. Carlo has been contacted by NEJM and his paper has been selected to have an accompanying CME activity.

We do not as yet have a target publication date.

Thanks for all your help

Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 2:26:00 PM

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
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Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Wednesday, March 24, 2010 2:20 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Thank you Stephanie,
Rochester looks good now.
Dale

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Wednesday, March 24, 2010 10:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; Phelps, Dale; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mlckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

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Tel. 301-496-0430

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archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]

Sent: Wednesday, March 24, 2010 9:51 AM

To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MICKey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa

Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]

Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Importance: High

Hi ALL-

Attached are the two SUPPORT paper mastheads for authorship and the boilerplates.

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Also, Dr. Carlo has been contacted by NEJM and his paper has been selected to have an accompanying CME activity.

We do not as yet have a target publication date.

Thanks for all your help

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Thursday, March 25, 2010 9:14:00 AM

From: Poindexter, Brenda B [mailto:bpindex@iupui.edu]
Sent: Thursday, March 25, 2010 9:14 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Both papers are correct for Indiana –
Thanks, Brenda

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Poindexter, Brenda B; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
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From: Shankaran, Seetha
To: Archer, Stephanie (NIH/NICHD) [E]
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 5:22:42 PM

Stephanie
Wayne State is fine
Seetha

Seetha Shankaran, MD
Professor of Pediatrics
Wayne State University School of Medicine
Director, Division of Neonatal/Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital
313-745-1436 (o)
313-745-5867 (f)
sshankar@med.wayne.edu

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Wednesday, March 24, 2010 1:34 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; Sood, Beena; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Shankaran, Seetha; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

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Tel. 301-496-0430
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archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]

Sent: Wednesday, March 24, 2010 9:51 AM

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Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]

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To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 2:25:47 PM

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Fanaroff, Avroy [mailto:Avroy.Fanaroff@JHhospitals.org]
Sent: Wednesday, March 24, 2010 2:19 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Looks OK to me
Thanks
Avroy

From: Archer, Stephanie (NIH/NICHD) [E] [mailto:archerst@mail.nih.gov]
Sent: Wednesday, March 24, 2010 1:34 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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Stephanie

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Sent: Wednesday, March 24, 2010 9:51 AM

To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa

Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]

Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Importance: High

Hi ALL-

Attached are the two SUPPORT paper mastheads for authorship and the boilerplates.

I request that the site PI's please look at this and tell me by Thursday, March 25 if any additional changes are warranted.

Also, Dr. Carlo has been contacted by NEJM and his paper has been selected to have an accompanying CME activity.

We do not as yet have a target publication date.

Thanks for all your help

Rose

Visit us at www.UHhospitals.org.

The enclosed information is STRICTLY CONFIDENTIAL and is intended for the use of the addressee only. University Hospitals and its affiliates disclaim any responsibility for unauthorized disclosure of this information to anyone other than the addressee.

Federal and Ohio law protect patient medical information, including psychiatric_disorders, (H.I.V) test results, A.I.Ds-related conditions, alcohol, and/or drug_dependence or abuse disclosed in this email. Federal regulation (42 CFR Part 2) and Ohio Revised Code section 5122.31 and 3701.243 prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: Krisa Van Meurs
To: Archer, Stephanie (NIH/NICHD) [E]
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ****REVIEW NEJM SUPPORT papers | author list and boilerplates****
Date: Wednesday, March 24, 2010 2:03:44 PM

Hi Stephanie and Rose,

For the masthead, can footnote 16 (Carlo manuscript) and 15 (Finer manuscript) be changed to:

Department of Pediatrics, Division of Neonatal and Developmental Medicine, Stanford University School of Medicine and Lucile Packard Children's Hospital, Palo Alto, CA

The boilerplate looks fine.

Many thanks,

Krisa

>As many of you have pointed out, I had some
> duplications between the authors and having
> their names in the boilerplate. I have corrected
> that in the attached files. Please let Rose and
> I know by tomorrow of any additional changes you
> need make.

>

>Stephanie

>

>Stephanie Wilson Archer
>The Eunice Kennedy Shriver
>National Institute of Child Health and Human Development
>Pregnancy & Perinatology Branch
>6100 Executive Boulevard, Room 4B03
>Rockville, MD 20852
>
>Tel. 301-496-0430
>Fax 301-496-3790
><<mailto:archerst@mail.nih.gov>>archerst@mail.nih.gov

>

>From: Higgins, Rosemary (NIH/NICHD) [E]
>Sent: Wednesday, March 24, 2010 9:51 AM
>To: Finer, Neil; 'Rich, Wade'; Gantz, Marie;
>Poole, W. Kenneth; 'Nancy Newman';
>(susie.buchter@oz.ped.emory.edu); Laroia,
>Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz';
>Vivek Narendran; 'Sood, Beena'; 'Michael
>O'Shea'; vineet.bhandari@yale.edu; Anthony
>Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda
>Morris; (Luc.Brion@UTSouthwestern.edu);
>(rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das;
>alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad

>Yoder (Bradley.yoder@hsc.utah.edu); Brenda
>Poindexter; Carlo Waldemar (E-mail);
>cotte010@mc.duke.edu; Dennis Wallace; Ed Bell;
>Ed Donovan; Ehrenkranz Richard (E-mail); Ivan
>Frantz (ifrantz@tuftsmedicalcenter.org);
>Kennedy, Kathleen A; Kristi Watterberg; Kurt
>Schibler [kurt.schibler@cchmc.org]; Matthew
>Bizzarro; Michelle Walsh; Mickey Caplan; Oh
>William (E-mail); Pablo Sanchez; Roger Faix;
>Ronald GOLdberg; Seetha Shankaran; Stevenson
>David (E-mail); Stoll Barbara (E-mail); Tyson
>Jon (E-mail); VanMeurs, Krisa
>Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
>Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
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>accompanying CME activity.

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>Thanks for all your help

>
>Rose

>
>
>Content-Type: application/msword;
> name="Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc"
>Content-Description: Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc
>Content-Disposition: attachment;
> filename="Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc";
> size=72704; creation-date="Wed, 24 Mar 2010 09:16:51 GMT";
> modification-date="Wed, 24 Mar 2010 13:24:46 GMT"

>
>Attachment converted: Macintosh HD:Boilerplate,
>Finer, #52E20A.doc (WDBN/«IC») (0052E20A)
>Content-Type: application/msword;
> name="Boilerplate, Carlo, SUPPORT Oximetry, 2010-03-24.doc"
>Content-Description: Boilerplate, Carlo, SUPPORT Oximetry, 2010-03-24.doc
>Content-Disposition: attachment;
> filename="Boilerplate, Carlo, SUPPORT
>Oximetry, 2010-03-24.doc"; size=73216;
> creation-date="Wed, 24 Mar 2010 09:04:39 GMT";
> modification-date="Wed, 24 Mar 2010 13:24:55 GMT"

>
>Attachment converted: Macintosh HD:Boilerplate,
>Carlo, #52E20B.doc (WDBN/«IC») (0052E20B)

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 1:40:24 PM

Stephanie Wilson Archer

The Eunice Kennedy Shriver

National Institute of Child Health and Human Development

Pregnancy & Perinatology Branch

6100 Executive Boulevard, Room 4B03

Rockville, MD 20852

Tel. 301-496-0430

Fax 301-496-3790

archerst@mail.nih.gov

From: Barbara Stoll [mailto:Barbara.Stoll@oz.ped.emory.edu]
Sent: Wednesday, March 24, 2010 1:38 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

AOK

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair
Department of Pediatrics, Emory University School of Medicine
President and CEO, Emory-Children's Center
SVP and Chief Academic Officer, Children's Healthcare of Atlanta
2015 Uppergate Dr
Atlanta GA 30022
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

Confidential - Please do not forward.

This message is for the designated recipient only and may contain privileged or confidential information. If you have received it in error, please notify the sender immediately and delete the original.

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@NIH/NICHD)
To: "Shankaran, Seetha"
Cc: [Archer, Stephanie \(NIH/NICHD\) \[E\]](mailto:Archer.Stephanie@NIH/NICHD)
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 1:29:00 PM

Correct
We will fix

Rose

From: Shankaran, Seetha [<mailto:sshankar@med.wayne.edu>]
Sent: Wednesday, March 24, 2010 1:26 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

Rose

Since Beena is listed as author, I think she should not be in boiler plate right
Seetha

Seetha Shankaran, MD
Professor of Pediatrics
Wayne State University School of Medicine
Director, Division of Neonatal/Perinatal Medicine
Children's Hospital of Michigan and
Hutzel Women's Hospital
313-745-1436 (o)
313-745-5867 (f)
sshankar@med.wayne.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman';
(susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek
Narendran; Sood, Beena; 'Michael O`Shea'; vineet.bhandari@yale.edu; Anthony Piazza
(Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu);
(rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad
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(ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler
(kurt.schibler@cchmc.org); Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail);
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Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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We do not as yet have a target publication date.

Thanks for all your help

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Phelps, Dale"
Cc: "Zaterka-Baxter, Kristin"; Archer, Stephanie (NIH/NICHD) [E]; "Reubens, Linda"
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 12:37:00 PM

We will fix these – we had one master but inadvertently names were duplicated when it was split into two papers

Thanks
Rose

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Wednesday, March 24, 2010 12:31 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Reubens, Linda
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Hi Rose,

Query:

Authors in the Masthead are listed again in the Boilerplate on both papers. I thought we had decided that authors in the Masthead are NOT to be listed again in the Masthead. I have lighted and done 'strike out' for these for Rochester.

>>> I checked on some of the other centers, and the listings are NOT consistent throughout the boilerplate.

Some repeat the masthead authors in the Boilerplate, and others do not.

If you want me to proof throughout for this, please let me know.

Changes:

1. I inadvertently left out our Department on both papers, and have put it in now on each masthead. Highlighted in green for you to find easily.
2. Finer: SUPPORT CPAP --- Gary Markowitz belongs only on the Carlo oximetry paper, not on the Ventilation Paper.

Dale Phelps
for the University of Rochester

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 6:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; Phelps, Dale; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler (kurt.schibler@cchmc.org); Matthew Bizzarro; Michelle Walsh; Mlckey Caplan; Oh William (E-mail);

Pablo Sanchez; Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll
Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

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Also, Dr. Carlo has been contacted by NEJM and his paper has been selected to
have an accompanying CME activity.

We do not as yet have a target publication date.

Thanks for all your help

Rose

From: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT | disclosure statement
Date: Wednesday, March 24, 2010 12:27:25 PM

No one, except Krisa, mentioned any other institution on their disclosure forms.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 12:26 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT | disclosure statement

Agree unless the money came in through some other source and the institution used it for travel

-----Original Message-----

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 12:25 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT | disclosure statement

There were 2 PIs that listed their own institutions as contributing funds for travel. I didn't include that in the disclosure. Seemed unnecessary, since it's obvious your own employer would be contributing in some way, shape or form.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 9:57 AM
To: Archer, Stephanie (NIH/NICHD) [E]; 'Wally Carlo, M.D.'
Subject: RE: SUPPORT | disclosure statement
Importance: High

Wally - see below - is this ok and do we even need to include the part about Massimo??

Thanks
Rose

-----Original Message-----

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 9:55 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT | disclosure statement

I mirrored this after the Phototherapy disclosure statement:

Supported by grants from the National Institutes of Health and from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, which provided overall oversight for study conduct. All data analyses and interpretation were done independently of the funding agency.

Participating centers purchased pulse oximeters from Masimo Radical Pulse Oximeter, Irvine, CA. Masimo customized the oximeters to mask the oxygenation ranges from clinical and study personnel during the intervention. Masimo played no role in the study design, data collection, data analysis, or manuscript preparation or revision.

Dr. Van Meurs reports receiving reimbursement for travel expenses from Ikaria Holdings, Inc. No other potential conflict of interest relevant to this article was reported.

We thank our medical and nursing colleagues and the infants and their parents.

We should use the same disclosure statement for Neil's paper.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 24, 2010 9:12 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Cc: 'Wally Carlo, M.D.'
Subject: FW: New England Journal of Medicine 09-11781.R2
Importance: High

Stephanie-

Can you draft a disclosure statement for the saturation paper to include a financial disclosure (statement of any author's relevant financial relationships or attestation of no relevant financial relationships) appear with the article for all the authors using the information from Section 3? We need to turn this around today.

Thanks
Rose

-----Original Message-----

From: Wally Carlo, M.D. [<mailto:WCarlo@peds.uab.edu>]
Sent: Tuesday, March 23, 2010 4:21 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: New England Journal of Medicine 09-11781.R2

Rose:

This is great news.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[<mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com>] On Behalf Of babel@nejm.org
Sent: Tuesday, March 23, 2010 3:08 PM
To: Wally Carlo, M.D.
Subject: New England Journal of Medicine 09-11781.R2

Re: 09-11781.R2 - A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Dear Dr. Carlo:

Your Journal article has been selected to have an accompanying CME activity. Consequently, the Accreditation Council for Continuing Medical Education (AACME) requires that a financial disclosure (statement of any author's relevant financial relationships or attestation of no relevant financial relationships) appear with the article.

As the corresponding author, we ask that you draft a disclosure statement for your manuscript based on the information in the submitted disclosure forms (attached). The statement should specify the type of relationships (e.g., consulting, paid speaking, grant support, equity, patents) each author has with each company. The information should be consistent with the authors' signed financial disclosure forms.

Section 2 pertains to the funding for the paper itself, which I believe is mentioned elsewhere in the paper, so you should pay particular attention to the information listed in Section 3 of the forms.

Let me know if you have any further questions. Please email the completed statement to me via email.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

From: Archer, Stephanie (NIH/NICHD) [E]
To: "Wally Carlo, M.D."; Higgins, Rosemary (NIH/NICHD) [E]
Cc: kzaterka@rti.org
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 12:23:15 PM

I've double-checked that now, as others have also pointed it out.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Wednesday, March 24, 2010 11:46 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]; kzaterka@rti.org
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Rose:

Ambal is listed both in the authors and acknowledgement. He can be taken out of the acknowledgement section. The same duplication of names occurs with almost half of the main authors.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 8:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu);

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From: Frantz, Ivan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 12:17:49 PM

Looks fine.

Ivan D. Frantz, III, M.D.
Professor of Pediatrics
Tufts University School of Medicine

Tufts Medical Center Box 44
800 Washington St.
Boston, MA 02111

617 636 5322

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alatook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Frantz, Ivan; Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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To: "Bell, Edward"; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 12:14:20 PM

Thanks! I've double-checked the list and (hopefully) eliminated all of the duplications.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Bell, Edward [mailto:edward-bell@uiowa.edu]
Sent: Wednesday, March 24, 2010 11:10 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Some but not all authors are also listed in Acknowledgements, for example Finer and Bell but not Carlo.
Shouldn't we be consistent?

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 8:51 AM
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We do not as yet have a target publication date.

Thanks for all your help

Rose

From: [Kennedy, Kathleen A](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 11:15:13 AM

Looks good to us.

Kathleen A. Kennedy, MD, MPH
Richard W. Mithoff Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
Director, MS in Clinical Research Degree Program
UT-Houston Medical School
6431 Fannin, Suite 2.106
Houston, TX 77030
713 500-6708

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 24, 2010 8:51 AM
To: 'Finer, Neil'; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler (kurt.schibler@cchmc.org); Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson, Jon E; VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

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Rose

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@nih.gov)
To: "Kennedy, Kathleen A"
Cc: [Archer, Stephanie \(NIH/NICHD\) \[E\]](mailto:Archer.Stephanie@nih.gov)
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 11:15:00 AM

FABULOUS AND THNAKS FOR YOUR PATIENCE WITH THIS!!!

From: Kennedy, Kathleen A [mailto:Kathleen.A.Kennedy@uth.tmc.edu]
Sent: Wednesday, March 24, 2010 11:15 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Looks good to us.

Kathleen A. Kennedy, MD, MPH
Richard W. Mithoff Professor of Pediatrics
Director, Division of Neonatal-Perinatal Medicine
Director, MS in Clinical Research Degree Program
UT-Houston Medical School
6431 Fannin, Suite 2.106
Houston, TX 77030
713 500-6708

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Sent: Wednesday, March 24, 2010 8:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; vineet.bhandari@yale.edu; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@ccchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson, Jon E; VanMeurs, Krisa
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Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Bell, Edward"
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 11:11:00 AM

If someone is an author, they should NOT appear in the boilerplate – we will fix this

Thanks
Rose

From: Bell, Edward [mailto:edward-bell@uiowa.edu]
Sent: Wednesday, March 24, 2010 11:10 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Some but not all authors are also listed in Acknowledgements, for example Finer and Bell but not Carlo. Shouldn't we be consistent?

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 8:51 AM
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
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Thanks for all your help

Rose

From: Roger Faix
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 11:01:42 AM

Both sets of mastheads and boilerplates look fine to me.

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 7:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O`Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Bradley Yoder; Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

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Thanks for all your help

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:43:00 AM
Importance: High

-----Original Message-----

From: Krisa Van Meurs [<mailto:vanmeurs@stanford.edu>]
Sent: Wednesday, March 24, 2010 10:26 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Importance: High

Hi Rose,

The boilerplate looks fine, but I would request that footnote 16 (Carlo manuscript) and 15 (Finer manuscript) read "Department of Pediatrics, Division of Neonatal and Developmental Medicine, Stanford University School of Medicine and Lucile Packard Children's Hospital, Palo Alto, CA".

Many thanks,

Krisa

>Hi ALL-
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>authorship and the boilerplates. I request that
>the site PI's please look at this and tell me by
>Thursday, March 25 if any additional changes are
>warranted.
>
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>his paper has been selected to have an
>accompanying CME activity.
>
>We do not as yet have a target publication date.
>
>Thanks for all your help
>
>Rose
>
>Content-Type: application/msword;
> name="Boilerplate, Carlo, SUPPORT Oximetry, 2010-03-24.doc"
>Content-Description: Boilerplate, Carlo, SUPPORT Oximetry, 2010-03-24.doc
>Content-Disposition: attachment;
> filename="Boilerplate, Carlo, SUPPORT
>Oximetry, 2010-03-24.doc"; size=74752;
> creation-date="Wed, 24 Mar 2010 09:04:39 GMT";
> modification-date="Wed, 24 Mar 2010 09:51:10 GMT"
>

>Attachment converted: Macintosh HD:Boilerplate,
>Carlo, #52DFB1.doc (WDBN/«IC») (0052DFB1)
>Content-Type: application/msword;
> name="Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc"
>Content-Description: Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc
>Content-Disposition: attachment;
> filename="Boilerplate, Finer, SUPPORT Ventilation, 2010-03-24.doc";
> size=69120; creation-date="Wed, 24 Mar 2010 09:32:52 GMT";
> modification-date="Wed, 24 Mar 2010 09:51:10 GMT"
>
>Attachment converted: Macintosh HD:Boilerplate,
>Finer, #52DFB2.doc (WDBN/«IC») (0052DFB2)

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:35:00 AM

From: Laptook, Abbot [mailto:ALaptook@WIHRI.org]
Sent: Wednesday, March 24, 2010 10:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

No additional changes from Brown. Tx, AL

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; Laptook, Abbot; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
Subject: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
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Rose

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this e-mail is prohibited. If you have received this e-mail in error, please notify sender by reply e-mail and delete this message and any attachment(s) immediately. Thank you for your consideration in this matter.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:25:00 AM

From: Michael O`Shea [mailto:moshea@wfubmc.edu]
Sent: Wednesday, March 24, 2010 10:13 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Rose,

Information for Wake Forest is correct

Thank you

Mike

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; Michael O`Shea; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:14:00 AM

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Wednesday, March 24, 2010 10:00 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Can my middle initial please be added so that it reads "Marie G. Gantz." This was added before but is not in the versions that were sent in this email.

Thanks,
Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; 'vineet.bhandari@yale.edu'; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Das, Abhik; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Wallace, Dennis; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); [SCRN] Stoll, Barbara; Tyson Jon (E-mail); VanMeurs, Krisa
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To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:13:00 AM

-----Original Message-----

From: Richard Ehrenkranz [<mailto:richard.ehrenkranz@yale.edu>]
Sent: Wednesday, March 24, 2010 10:08 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Vineet Bhandari
Subject: Re: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****

Rose:

The listings are correct. However, in previous versions Vineet was listed as an author in Neil's paper, with me listed in the Acknowledgements, while I was listed as an author in Wally's paper, with Vineet listed in the Acknowledgements. In these attached versions, the authorship is correct, but now both of us are listed in each boilerplate.
Richard

Higgins, Rosemary (NIH/NICHD) [E] wrote:

>
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> Thanks for all your help
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> Rose
>

--

Richard A. Ehrenkranz, MD
Department of Pediatrics
Yale University School of Medicine
333 Cedar Street
PO Box 208064
New Haven, CT 06520-8064
tele: 203-688-2320
fax: 203-688-5426

The information contained in this email may be privileged and confidential. If you are the intended recipient, you must maintain this message in a secure and confidential manner. If you are not the intended recipient, please notify the sender immediately and destroy this message. Thank you.

From: Kurt Schibler
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:12:54 AM

Rose,
The author masthead and acknowledgment boilerplate looks fine for Cincinnati. Thanks,
Kurt

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 3/24/2010 9:51 AM >>>

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From: Walsh, Michele
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: *****REVIEW NEJM SUPPORT papers | author list and boilerplates*****
Date: Wednesday, March 24, 2010 10:09:16 AM

For oxygen sat paper please add Arlene Zadell RN and Julie DiFiore BS for CWRU boilerplate.

Michele Walsh
beeper 30642
Ph 216 844 3759

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 24, 2010 9:51 AM
To: Finer, Neil; 'Rich, Wade'; Gantz, Marie; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); Laroia, Nirupama; 'Phelps, Dale'; 'Duara, Shahnaz'; Vivek Narendran; 'Sood, Beena'; 'Michael O` Shea'; vineet.bhandari@yale.edu; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); Brenda Morris; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'; Archer, Stephanie (NIH/NICHD) [E]
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Rose

Visit us at www.UHhospitals.org.

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Federal and Ohio law protect patient medical information, including psychiatric_disorders,

(H.I.V) test results, A.I.Ds-related conditions, alcohol, and/or drug_dependence or abuse disclosed in this email. Federal regulation (42 CFR Part 2) and Ohio Revised Code section 5122.31 and 3701.243 prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: [Webb, Robin E.](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: 3rd revision of MILK study for protocol review
Date: Wednesday, March 24, 2010 9:45:53 AM

I sent out an email to poll for the SUPPORT secondary study to evaluate intermittent hypoxia in preterm infants, I'll use the availability for this one as well. Would you want to do them at the same time if there is a 2 hour block of time that works?

Thanks,
Robin

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 24, 2010 8:49 AM
To: Webb, Robin E.; 'Richard Ehrenkranz'; 'Brenda Poindexter'; 'Tyson, Jon E'; ifrantz@tuftsmedicalcenter.org; 'ROGER.FAIX@HSC.UTAH.EDU'; 'Kurt Schibler [kurt.schibler@cchmc.org]'; Das, Abhik; Wallace, Dennis; 'Kristi Watterberg'
Cc: Zaterka-Baxter, Kristin; Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; Huitema, Carolyn Petrie
Subject: FW: 3rd revision of MILK study for protocol review

Here is the MILK study for protocol review

Robin - can we try to get this done in April?
Thanks
Rose

-----Original Message-----

From: Colaizy, Tarah T [<mailto:tarah-colaizy@uiowa.edu>]
Sent: Wednesday, March 24, 2010 12:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: 3rd revision of MILK study for protocol review

Rose:

Here is the official third revision of the protocol, with a cover letter.

Please pass on to protocol review. Do you think there is a chance of presenting this at the May meeting, if protocol review passes it? (or before by call, I don't care how, I just would love to get a yes or no on this!)

Tarah

--

Tarah Colaizy, MD, MPH
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From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Cc: ["Wally Carlo, M.D."](#)
Subject: FW: New England Journal of Medicine 09-11781.R2
Date: Wednesday, March 24, 2010 9:12:00 AM
Attachments: [Carlo-0911781-disclosures.pdf](#)
Importance: High

Stephanie-

Can you draft a disclosure statement for the saturation paper to include a financial disclosure (statement of any author's relevant financial relationships or attestation of no relevant financial relationships) appear with the article for all the authors using the information from Section 3? We need to turn this around today.

Thanks
Rose

-----Original Message-----

From: Wally Carlo, M.D. [<mailto:WCarlo@peds.uab.edu>]
Sent: Tuesday, March 23, 2010 4:21 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: New England Journal of Medicine 09-11781.R2

Rose:

This is great news.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[<mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com>] On Behalf Of babel@nejm.org
Sent: Tuesday, March 23, 2010 3:08 PM
To: Wally Carlo, M.D.
Subject: New England Journal of Medicine 09-11781.R2

Re: 09-11781.R2 - A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Dear Dr. Carlo:

Your Journal article has been selected to have an accompanying CME activity. Consequently, the Accreditation Council for Continuing Medical Education (AACME) requires that a financial disclosure (statement of any author's relevant financial relationships or attestation of no relevant financial relationships) appear with the article.

As the corresponding author, we ask that you draft a disclosure statement for your manuscript based on the information in the submitted disclosure forms (attached). The statement should specify the type of relationships (e.g., consulting, paid speaking, grant support, equity, patents) each author has with each company. The information should be consistent with the authors' signed financial disclosure forms.

Section 2 pertains to the funding for the paper itself, which I believe is mentioned elsewhere in the paper, so you should pay particular attention to the information listed in Section 3 of the forms.

Let me know if you have any further questions. Please email the completed statement to me via email.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

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2. The work under consideration for publication.

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3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Namasivayam

Surname:
(or last)

Ambalavanan

Effective Date:

01-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH	Grant funding	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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Section 1. Identifying Information.

Given Name: (or first)

Surname: (or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH (NICHD)		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Travel funded from the NIH grant		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
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							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	University of Iowa	The University reimburses, with funds from my NIH grant, my travel costs to attend the meetings of the NICHD Neonatal Research Network	Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Waldemar

Surname:
(or last)

Carlo

Effective Date:

24-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Given Name: (or first)

Surname: (or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	As a member site of the NICHD Neonatal Research Network Duke receives a base award which includes support for a study coordinator and the Principle investigator and alternate PI. There is also indirect support that goes to the institution. The NICHD also provided additional financial support per patient enrolled to help cover costs of research staff enrolling patients and conducting the study.	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH FUNDING		Del x
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5. Nonfinancial associations.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: (or first)

Surname: (or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Yale was a participating center	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +

**Use this section to provide any needed explanation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD Neonatal Research Network	Capitated payment for enrollment, data collection, day to day conduct of study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD Neonatal Research Network		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Neil

Surname:
(or last)

Finer

Effective Date:

Feb 1 2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

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- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Save Form



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2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eunice Kennedy Shriver National Institute of Child Health and Human Development		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:
 (or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
 Yes, specify nature of compensation

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del x
							Add +
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment support at NICHD		Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			Del x
							Add +

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Employee and Program Scientist	Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:

(or first)

(or last)

Effective Date:

2004-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

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Yes, specify nature of compensation

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
 Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

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2. The work under consideration for publication.

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3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Nirupama

Surname:
(or last)

Laroia

Effective Date:

19-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar A Carlo

Manuscript Title:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH- NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Study related meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +

**Use this section to provide any needed explanation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Section 1. Identifying Information.

Given Name: (or first)

Surname: (or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funded trial	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD/UT Houston	Expenses for travel	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
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							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Vivek

Surname:
(or last)

Narendran

Effective Date:

25-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Dr Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

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Yes, specify nature of compensation

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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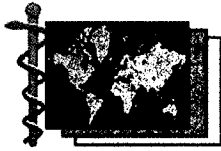
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5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Nancy

Surname:
(or last)

Newman

Effective Date:

24-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Wally Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: (or first)

Surname: (or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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 (or first) (or last) Format example: 07-August-2008

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Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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- No
 Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH / NICHD	5% PI support, Coordinator effort, supplies	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH/NICHD	Travel for planning and monitoring meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD/NIH	Funds to purchase equipment for the study	Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD		Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD		Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
 Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
 Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

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Save Form



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1. Identifying information.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Brenda

Surname:
(or last)

Poindexter

Effective Date:

24-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Wally Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

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No

Yes, specify nature of compensation

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Kenneth

Surname:
(or last)

Poole

Effective Date: 26-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name: Waldemar Carlo

Manuscript Title: A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it): 09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Section 1. Identifying Information.

Given Name:
(or first)

Wade

Surname:
(or last)

Rich

Effective Date:

12Feb2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
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						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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Section 1. Identifying Information.

Given Name: Surname: Effective Date:
(or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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 Yes, specify nature of compensation

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	U10HD40689	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	U10HD40689	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

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3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:
 (or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
 Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Cincinnati Site Principal Investigator to attend Steering Committee Meeting	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Study Oximeters Provided by Neonatal Network	Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Section 1. Identifying Information.

Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHHD	Funding for study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +

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If you have more than one relationship, click "Add +" to add a row. Click "Del ×" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

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Given Name: Surname: Effective Date:
 (or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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- No
 Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Ikaria		Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Michele

Surname:
(or last)

Walsh

Effective Date:

26-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Case Western REserve Univ		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Case Western Reserve Univ		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

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- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Save Form



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Kristi

Surname:
(or last)

Watterberg

Effective Date:

26-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it):

09-11781

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No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

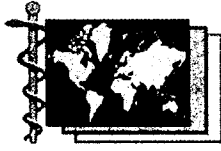
**Use this section to provide any needed explanation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Save Form



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Bradley

Surname:
(or last)

Yoder

Effective Date:

29 Jan 2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

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No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH, NICHD	As member of Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH, NICHD	Same	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH, NICHD	Standardized oxygen monitors	Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT FINAL AUTHORS + boilerplate for individual papers
Date: Wednesday, March 24, 2010 8:43:00 AM

Do you have the two support final authorship and boilerplates for each paper separately? I would like them by tomorrow so I have them with me in case the galleys arrive in the next 10 days

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Abel, Brendan
To: "Wally Carlo, M.D."
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: New England Journal of Medicine 09-11781.R2
Date: Tuesday, March 23, 2010 4:23:50 PM

Thanks very much, Wally. And just to clarify, after the disclosure statement at the end of the text, there will be a sentence notifying the readers that the full version of the forms are available online. (I don't want you to think all of the collecting and correcting will go to waste.)

Brendan

-----Original Message-----

From: Wally Carlo, M.D. [<mailto:WCarlo@peds.uab.edu>]
Sent: Tuesday, March 23, 2010 4:21 PM
To: Abel, Brendan
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: New England Journal of Medicine 09-11781.R2

Brendan:

Great! I will work on it right away.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
1700 6th Avenue South
176F Suite 9380R
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[<mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com>] On Behalf Of babel@nejm.org
Sent: Tuesday, March 23, 2010 3:08 PM
To: Wally Carlo, M.D.
Subject: New England Journal of Medicine 09-11781.R2

Re: 09-11781.R2 - A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Dear Dr. Carlo:

Your Journal article has been selected to have an accompanying CME activity. Consequently, the Accreditation Council for Continuing Medical Education (AACME) requires that a financial disclosure (statement of any author's relevant financial relationships or attestation of no relevant financial relationships) appear with the article.

As the corresponding author, we ask that you draft a disclosure statement for your manuscript based on the information in the submitted disclosure forms (attached). The statement should specify the type of relationships (e.g., consulting, paid speaking, grant support, equity, patents) each author has with each company. The information

should be consistent with the authors' signed financial disclosure forms.

Section 2 pertains to the funding for the paper itself, which I believe is mentioned elsewhere in the paper, so you should pay particular attention to the information listed in Section 3 of the forms.

Let me know if you have any further questions. Please email the completed statement to me via email.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

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From: [Webb, Robin E.](mailto:Webb_Robin_E)
To: bpoindex@iupui.edu; adas@rti.org; [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins_Rosemary_(NIH/NICHD)_[E]); ifrantz@tuftsmedicalcenter.org; jon.e.tyson@uth.tmc.edu; kurt.schibler@cchmc.org; kwatterberg@salud.unm.edu; richard.ehrenkranz@yale.edu; Roger.Faix@hsc.utah.edu; [Wallace, Dennis](mailto:Wallace_Dennis)
Cc: [Irene, Amanda](mailto:Irene_Amanda); [Webb, Robin E.](mailto:Webb_Robin_E); debra.camputaro@yale.edu; sharon.gough@hsc.utah.edu; [Archer, Stephanie \(NIH/NICHD\) \[E\]](mailto:Archer_Stephanie_(NIH/NICHD)_[E]); [Cunningham, Meg](mailto:Cunningham_Meg); [Huitema, Carolyn Petrie](mailto:Huitema_Carolyn_Petrie); Nancy.M.Smith@uth.tmc.edu; [Zaterka-Baxter, Kristin](mailto:Zaterka-Baxter_Kristin)
Subject: Protocol review call
Date: Tuesday, March 23, 2010 2:24:53 PM

We need to schedule a protocol review call to discuss a SUPPORT secondary study to evaluate intermittent hypoxia in preterm infants. The protocol will be sent out shortly. Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Wed 4/7
Thurs 4/8
Fri 4/9

Mon 4/12
Tues 4/13

Mon 4/19
Tues 4/20
Wed 4/21
Thurs 4/22
Fri 4/23

Mon 4/26
Tues 4/27
Wed 4/28
Thurs 4/29
Fri 4/30

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Roger Faix"; "Brad Yoder (Bradley.yoder@hsc.utah.edu)"; "Anna Bodnar"; "(Karen.Osborne@hsc.utah.edu)";
"Shawna Baker"
Cc: "Gantz, Marie"
Subject: SUPPORT FU OUTCOMES
Date: Thursday, March 18, 2010 2:10:00 PM

**CONGRATULATIONS!!
WE HAVE NO MISSING SUPPORT FU OUTCOMES FROM
YOUR SITE AS OF THIS WEEK'S DATA ENTRY.**

**THANKS FOR ALL THE EFFORT AND KEEP UP THE GOOD
WORK!!!!**

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ivan Frantz (ifrantz@tuftsmedicalcenter.org)"; "Brenda Mackinnon (bmackinnon@tuftsmedicalcenter.org)";
"emcgowan@tuftsmedicalcenter.org"; "Furey, Anne M"
Cc: "Gantz, Marie"
Subject: SUPPORT FU OUTCOMES
Date: Thursday, March 18, 2010 2:09:00 PM

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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ronald N. Goldberg"; "Ricki F. Goldstein"; "cotte010@mc.duke.edu"; "Sandra Grimes"; "Kimberley Fisher"; "kim.lutz@duke.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT FU OUTCOMES
Date: Thursday, March 18, 2010 2:08:00 PM

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**THANKS FOR ALL THE EFFORT AND KEEP UP THE GOOD
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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo Sanchez"; "Roy.Heyne@utsouthwestern.edu"; "Nancy Miller"; "Diana Vasil"; "Lizette Torres"
Cc: "Gantz, Marie"
Subject: SUPPORT FU OUTCOMES
Date: Thursday, March 18, 2010 2:07:00 PM

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YOUR SITE AS OF THIS WEEK'S DATA ENTRY.**

**THANKS FOR ALL THE EFFORT AND KEEP UP THE GOOD
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Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ehrenkranz Richard (E-mail)"; "monica.konstantino@yale.edu"; "Matthew Bizarro"; "elaine.romano@yale.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT FU OUTCOMES
Date: Thursday, March 18, 2010 2:07:00 PM

**CONGRATULATIONS!!
WE HAVE NO MISSING SUPPORT FU OUTCOMES FROM
YOUR SITE AS OF THIS WEEK'S DATA ENTRY.**

**THANKS FOR ALL THE EFFORT AND KEEP UP THE GOOD
WORK!!!!**

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wcarlo@peds.uab.edu"
Subject: Fw: Dr. Finer's Availability - SUPPORT PAPERS!!!
Date: Thursday, March 11, 2010 5:59:08 PM

Can you do 4-5 on monday??

From: Martinez, Fernando <fmartinez@ucsd.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil <nfiner@ucsd.edu>; wcarlo@uab.edu <wcarlo@uab.edu>
Cc: 'Lila Guterman' <lguterman@palladianpartners.com>; Bock, Robert (NIH/NICHD) [E]
Sent: Thu Mar 11 17:45:07 2010
Subject: Dr. Finer's Availability - SUPPORT PAPERS!!!

Dear Dr. Higgins,

Please see below for Dr. Finer's availability:

March 12 – anytime before 1 PM ET: Not available, giving lecture in Mexico
March 15 – 4-5 pm et (1-2 pm pt): OK

Regards,
Fernando

Fernando I. Martinez
Administrative Supervisor
Assistant to Division Director, Dr. Neil N. Finer
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
402 Dickinson St., MPF 1-140
San Diego, CA 92103-8774
Telephone: 619.543.3759
Facsimile: 619.543.3812



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From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, March 11, 2010 11:04 AM
To: Finer, Neil; wcarlo@uab.edu; Martinez, Fernando
Cc: 'Lila Guterman'; Bock, Robert (NIH/NICHD) [E]
Subject: SUPPORT PAPERS!!!

Importance: High

Neil and Wally,

Our public affairs office is interested in discussing the two SUPPORT papers with you.

Are you available to speak with them (and me) by phone either:

March 12 – anytime before 1 PM ET

March 15 – 4-5 pm et

Let me know so I can set this up.

Thanks for all your help

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institutes of Health

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MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Boilerplate | SUPPORT
Date: Thursday, March 11, 2010 10:58:26 AM

I'm working on it right now.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, March 11, 2010 10:57 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: Boilerplate | SUPPORT

Do we have all of these??

-----Original Message-----

From: Pablo Sanchez [<mailto:Pablo.Sanchez@UTSouthwestern.edu>]
Sent: Monday, March 08, 2010 11:45 AM
To: Archer, Stephanie (NIH/NICHD) [E]; wcarlo@peds.uab.edu; Neil 'Finer'
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Boilerplate | SUPPORT

Hi Stephanie--please see below---sorry, they helped with both of the studies--Laura Grau goes only under the pulse ox/ ROP one and not CPAP--thanks--pablo

University of Texas Southwestern Medical Center at Dallas Parkland Health & Hospital System and Children's Medical Center Dallas (U10 HD40689, GCRC M01 RR633) - Charles R. Rosenfeld, MD; Walid A. Salhab, MD; Alicia Guzman; Gaynelle Hensley, RN; Melissa H. Lepps, RN; Nancy A. Miller, RN.

Diana M Vasil, RNC, NIC, James Allen, RRT, Araceli Solis, RRT, Melissa Martin, RN, Kerry Wilder, RN, Laura Grau, RN

>>> "Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov> 3/5/10 9:13 AM >>>
Pablo,

Please send us your complete list of names.

At the moment, I believe both manuscripts include:

University of Texas Southwestern Medical Center at Dallas Parkland Health & Hospital System and Children's Medical Center Dallas (U10 HD40689, GCRC M01 RR633) - Charles R. Rosenfeld, MD; Walid A. Salhab, MD;

Alicia Guzman; Gaynelle Hensley, RN; Melissa H. Lepps, RN; Nancy A. Miller, RN.

When we get the galleys, we will add:
Diana M Vasil, RNC, NIC

-----Original Message-----

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Thursday, March 04, 2010 7:16 PM
To: Pablo Sanchez; Archer, Stephanie (NIH/NICHD) [E]; wcarlo@peds.uab.edu
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Boilerplate | SUPPORT

I think we can add this to the galleys - It will not add length to the manuscript
Neil

-----Original Message-----

From: Pablo Sanchez [<mailto:Pablo.Sanchez@UTSouthwestern.edu>]
Sent: Thursday, March 04, 2010 2:07 PM
To: archerst@mail.nih.gov; wcarlo@peds.uab.edu; Finer, Neil
Cc: higginsr@mail.nih.gov
Subject: Re: Boilerplate | SUPPORT

Actually, I have been meaning to e-mail you about this-please include her in both-also if not too late, need to add a couple of others-sorry-pablo

Pablo -sent from Blackberry

214-648-3753 (office)

214-621-1068 (cell)

972-206-9021 (beeper)

-----Original Message-----

From: "Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov>
Cc: Rosemary (NIH/NICHD) [E] Higgins <higginsr@mail.nih.gov>
To: Wally Carlo(wcarlo@peds.uab.edu) <wcarlo@peds.uab.edu>
To: Neil Finer (nfiner@ucsd.edu) <nfiner@ucsd.edu>
Cc: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>

Sent: 3/4/2010 3:42:23 PM

Subject: RE: Boilerplate | SUPPORT

Hi Wally and Neil,

Were you able to add Diana to the boilerplate in the final versions of the NEJM papers?

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430

Fax 301-496-3790

archerst@mail.nih.gov<<mailto:archerst@mail.nih.gov>>

From: Archer, Stephanie (NIH/NICHD) [E]

Sent: Tuesday, February 02, 2010 2:43 PM

To: Wally Carlo (wcarlo@peds.uab.edu); Neil Finer (nfiner@ucsd.edu)
Cc: Higgins, Rosemary (NIH/NICHD) [E]; 'Pablo Sanchez (Pablo.Sanchez@UTSouthwestern.edu)'; Archer, Stephanie (NIH/NICHD) [E]
Subject: Boilerplate | SUPPORT

Hi Wally and Neil,

Pablo would like to add "Diana M Vasil, RNC, NIC" to the list of people in the acknowledgements for UT Southwestern.

When you get the galleys back, I can review the boilerplate information for you.

Thanks,

Stephanie

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov<<mailto:archerst@mail.nih.gov>>

From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: ["Rich, Wade"; Finer, Neil; Wally Carlo, M.D.](#)
Subject: RE: Change of authorship letters for NEJM
Date: Thursday, March 11, 2010 10:29:38 AM

Hi Rose,

Thanks for passing along. As I think I mentioned earlier, please be sure to take a close look at the title page and acknowledgements at the galley stage to be sure they reflect the most recent authorship list.

For now, you're all set.

Best,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 10, 2010 1:16 PM
To: 'Rich, Wade'; Abel, Brendan; Finer, Neil
Subject: RE: Change of authorship letters for NEJM

From: Rich, Wade [<mailto:wrich@ucsd.edu>]
Sent: Wednesday, March 10, 2010 12:54 PM
To: Abel, Brendan; Finer, Neil
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Change of authorship letters for NEJM
Importance: High

Hi Brendan,

Attached please find a .pdf file containing all of the author letters for the addition of Kathleen Kennedy, MD, MPH and the deletion of Brenda Morris, MD from the manuscript "Early CPAP versus Surfactant in Extremely Preterm Infants. One author, Dr. Laroia, has already faxed to NEJM directly.

Please feel free to contact me if you have any questions.

Thank you,

Wade

Wade Rich BSHS, RRT, CCRC
Research Coordinator - Neonatology
UCSD Medical Center
402 Dickinson St. Ste 1-140
San Diego, CA 92103-8774
Ph. 619-543-5375
FAX 619-543-3812

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 10, 2010 9:41 AM
To: Finer, Neil; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: Change of authorship letters for NEJM
Importance: High

Neil and Wade

Attached is a pdf with all except Dr. Laroia's letter (already faxed to NEJM directly) for deletion of Brenda and addition of Kathleen for the authors. You will need to add one from UCSD with both of your signatures and this can be emailed directly to Brendan Abel (babel@NEJM.org). If you could copy me on this email to Brendan, that would be great.

Thanks for your patience!!!
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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From: Walsh, Michele
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ***Urgent authorship issue for CPAP paper*****
Date: Wednesday, March 10, 2010 12:07:47 PM

He wasn't on it so it was ok.
I sent same day.

Michele Walsh
beeper 30642
Ph 216 844 3759

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 10, 2010 10:48 AM
To: Walsh, Michele
Subject: RE: ***Urgent authorship issue for CPAP paper*****

Yes,
I sent those out Friday – do you need me to resend??

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Walsh, Michele [mailto:Michele.Walsh@UHhospitals.org]
Sent: Monday, March 08, 2010 5:17 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ***Urgent authorship issue for CPAP paper*****

Av is still out of the country. Are acknowledgements included?

Michele Walsh
beeper 30642
Ph 216 844 3759

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 08, 2010 1:27 PM
To: 'Finer, Neil'; 'Wally Carlo, M.D.'; 'Michelle Walsh'; 'wrich@ucsd.edu'; 'Gantz, Marie'; 'alaptook@WIHRI.org'; 'Brad Yoder (Bradley.yoder@hsc.utah.edu)'; 'Roger Faix'; 'alaptook@WIHRI.org'; 'Poole Kenneth (E-mail)'; 'Bell, Edward'; 'Ed Donovan'; 'nxs5@cwru.edu'; 'Ivan Frantz (ifrantz@tuftsmedicalcenter.org)'; 'susie.buchter@oz.ped.emory.edu'; 'Pablo Sanchez'; 'Kennedy, Kathleen A'; 'nirupama_laroya@urmc.rochester.edu'; 'Brenda Poindexter'; 'cotte010@mc.duke.edu'; 'Duara, Shahnaz'; 'vivek.narendran@cchmc.org'; 'bsood@med.wayne.edu'; '(vineet.bhandari@yale.edu)'; 'Kristi Watterberg'; 'O'Shea, Michael'; 'VanMeurs, Krisa'; 'Das, Abhik'; 'Brenda Morris'
Cc: Johnson, Nichole (NIH/OD) [E]
Subject: ***Urgent authorship issue for CPAP paper*****
Importance: High

Hi

We have an authorship issue from UT Houston. Originally, Brenda was listed for both papers. Kathleen had told us that Brenda should be on the oximetry paper and Kathleen on the CPAP paper. When the manuscripts were submitted, Brenda was on both papers. In order to get the appropriate authors on each paper for UT Houston, NEJM requests that each co-author including the one being deleted and the one being added, as well as the remaining co-authors sign a statement for the editor.

Please insert your institution's letterhead on the attached letter and adjust the first paragraph to accurately reflect either I (one signature) or we (multiple signatures) from your site. It is necessary that you return the letter to NICHD by Tuesday March 9 via FAX (301-496-3790). Sign the letter and print the name(s). WE need all the authors to sign a letter.

Thanks for your patience. The goal is to get the authorship correct on the manuscripts.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT papers boilerplates
Date: Wednesday, March 10, 2010 10:53:00 AM

Do you have Pablo's changes to the boilerplate (can't recall if he sent this to you that started the whole process)

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, March 10, 2010 10:44 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT papers boilerplates

Of course!

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 10, 2010 10:36 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT papers boilerplates

Stephanie –

Can I send you all of the SUPPORT boilerplate changes? We will have a 24-48 hour turnaround time once we get our galleys from NEJM and we will need several "eyes" to look at this. When I spoke to the editorial office yesterday, they did not have an anticipated publication date. Can you prepare a "new" boilerplate with highlighted additions/deletions?? Let me know. There are not too many changes

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: ****Important NEJM acknowledgements*****
Date: Wednesday, March 10, 2010 10:51:00 AM

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Michael Cotten [mailto:cotte010@mc.duke.edu]
Sent: Monday, March 08, 2010 11:12 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Ronald N Goldberg
Subject: Re: ****Important NEJM acknowledgements*****

Duke is ok w/ the listing for the two papers.

mc

C. Michael Cotten MD MHS
Associate Professor of Pediatrics
Medical Director Neonatology Clinical Research
Duke University Medical Center
Box 2739 DUMC
Durham, NC 27710
2424 Erwin Road Suite 504
Durham, NC 27705
ph: 919-681-6024
fax: 919-681-6065
email: cotte010@mc.duke.edu

"Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov>

03/05/2010 09:18 AM

To "Finer, Neil" <nfiner@ucsd.edu>, "Duara, Shahnaz" <SDuara@med.miami.edu>, "Phelps, Dale" <Dale_Phelps@URMC.Rochester.edu>, "Michael O'Shea" <moshea@wfbmc.edu>, " (Luc.Brion@UTSouthwestern.edu)" <Luc.Brion@UTSouthwestern.edu>, " (rohls@unm.edu)" <rohls@unm.edu>, "aaf2@po.cwru.edu" <aaf2@po.cwru.edu>, Abhik Das <adas@rti.org>, "alaptook@WIHRI.org" <alaptook@WIHRI.org>, "Ambal (ambal@uab.edu)" <ambal@uab.edu>, "Brad Yoder (Bradley.yoder@hsc.utah.edu)" <Bradley.yoder@hsc.utah.edu>, Brenda Poindexter <bpoindexter@iupui.edu>, "Carlo Waldemar (E-mail)" <wcarlo@peds.uab.edu>, "cotte010@mc.duke.edu" <cotte010@mc.duke.edu>, Dennis Wallace <dwallace@rti.org>, Ed Bell <Edward-bell@uiowa.edu>, Ed Donovan <edward.donovan@cchmc.org>, "Ehrenkranz Richard (E-mail)" <richard.ehrenkranz@yale.edu>, "Ivan Frantz (ifrantz@tuftsmedicalcenter.org)" <ifrantz@tuftsmedicalcenter.org>, "Kennedy, Kathleen A" <Kathleen.A.Kennedy@uth.tmc.edu>, Kristi Watterberg <kwatterberg@salud.unm.edu>, "Kurt Schibler [kurt.schibler@cchmc.org]" <kurt.schibler@cchmc.org>, Matthew Bizzarro <matthew.bizzarro@yale.edu>, Michelle Walsh <mcw3@po.cwru.edu>, Mickey Caplan <mcaplan@northshore.org>, "Oh William (E-mail)" <william_oh@brown.edu>, Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>, "Poole Kenneth (E-mail)" <poo@rti.org>, Roger Faix <Roger.Faix@hsc.utah.edu>, Ronald Goldberg <goldb008@mc.duke.edu>, Seetha Shankaran <sshankar@med.wayne.edu>, "Stevenson David (E-mail)" <dstevenson@stanford.edu>, "Stoll Barbara (E-mail)" <barbara_stoll@oz.ped.emory.edu>, "Tyson Jon (E-mail)" <Jon.E.Tyson@uth.tmc.edu>, "VanMeurs, Krisa" <vanmeurs@leland.stanford.edu>

cc "Zaterka-Baxter, Kristin" <kzaterka@rti.org>
Subject ****Important NEJM acknowledgements*****

Hi,

It was brought to our attention that at least one site has a staff member missing on the acknowledgements section of the SUPPORT papers. I spoke with Brendan Abel, editorial assistant at NEJM this morning and we will be permitted to insert additional names into the acknowledgements section. He pointed out that no changes can be made to the manuscript without the approval of the editor so the attached papers are final.

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Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

[attachment "CarloSUPPORTFINAL (2).doc" deleted by Michael

Cotten/Pediatrics/mc/Duke] [attachment "FinerSUPPORTFinal (2).doc" deleted by Michael

Cotten/Pediatrics/mc/Duke]

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: ****Important NEJM acknowledgements*****
Date: Wednesday, March 10, 2010 10:51:00 AM

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Kurt Schibler [mailto:kurt.schibler@cchmc.org]
Sent: Monday, March 08, 2010 9:10 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: ****Important NEJM acknowledgements*****

Hi Rose,

For the Oximetry SUPPORT paper, on page 2, Vivek Narendran and Kurt Schibler are in Department of Pediatrics, Cincinnati Children's Hospital Medical Center and University of Cincinnati, Cincinnati, Ohio. On page 21, Vivek Narendran can be deleted from the Acknowledgment since he is an author on the paper.

For the CPAP SUPPORT paper on page 2, Vivek Narendran and Edward Donovan are in Department of Pediatrics, Cincinnati Children's Hospital Medical Center and University of Cincinnati, Cincinnati, Ohio. On page 19, Kurt Schibler should be added to the Acknowledgment and Edward Donovan can be deleted from since he is an author on the paper.

Thanks,
Kurt

Kurt Schibler, MD
Associate Professor of Pediatrics
Division of Neonatology, ML 7009
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, Ohio 45229
TEL: 513-636-3972
Pager: 513-736-5649
E-mail: kurt.schibler@cchmc.org

On 3/5/10 9:17 AM, "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> wrote:

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For overnight delivery use Rockville, MD 20852
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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: ****Important NEJM acknowledgements*****
Date: Wednesday, March 10, 2010 10:48:00 AM

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Laptook, Abbot [mailto:ALaptook@WIHRI.org]
Sent: Monday, March 08, 2010 2:40 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: ****Important NEJM acknowledgements*****

Rose

Can we add the following two RTs who helped make this study happen for the Brown/WIH site:

Susan Barnett RRT

Sarah Lillie RRT

I would list after Dan Gingras on both papers. Tx, AL

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 9:18 AM
To: 'Finer, Neil'; 'Duara, Shahnaz'; Phelps, Dale; 'Michael O` Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; Laptook, Abbot; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'
Subject: ****Important NEJM acknowledgements*****

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higginsr@mail.nih.gov

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From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: "[Irene, Amanda](#)"
Subject: RE: BPD/Oximetry minutes
Date: Wednesday, March 10, 2010 9:55:00 AM

Awesome
Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Irene, Amanda [<mailto:airene@rti.org>]
Sent: Wednesday, March 10, 2010 9:55 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: BPD/Oximetry minutes

Hi Rose,

I actually had Dennis look at them before I sent them to you! Great minds think alike..

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 10, 2010 9:52 AM
To: Irene, Amanda
Cc: Wallace, Dennis
Subject: RE: BPD/Oximetry minutes

Amanda, Please have Dennis look at these for accuracy. Also, change the title to SUPPORT SUBCOMMITTEE CALL.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Irene, Amanda [<mailto:airene@rti.org>]
Sent: Wednesday, March 10, 2010 9:30 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: BPD/Oximetry minutes

Hi Rose,

I've attached the minutes from the BPD/Oximetry call last week. Let me know if there are any changes!

Thanks!
Amanda

From: Abel, Brendan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Change of authorship
Date: Wednesday, March 10, 2010 9:39:59 AM

Great. Thank you!

I'm taking a half day today, so feel free to pass tomorrow AM if that makes life any easier for you.

Best,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 10, 2010 9:38 AM
To: Abel, Brendan
Subject: RE: Change of authorship

Great, Laroia was the only one we were missing – we will get you the rest before the end of the day.

Thanks for all your help!!
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Wednesday, March 10, 2010 9:28 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Change of authorship

Hi Rose,

In case it helps, I now have change of authorship forms from Laroia, Yoder, Faix and Laptook.

Brendan

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

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From: Phelps, Dale
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: not to leave it hanging
Date: Monday, March 08, 2010 9:24:13 PM

Hi Rose,

So the acknowledgments for SUPPORT CPAP are not left hanging for Rochester, I am NOT going to request any changes.

Dale

Dale Phelps
Professor of Pediatrics
30250 S.Highway 1
Gualala, CA 95445
Ph. (707) 897-9063

From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: Change of authorship
Date: Monday, March 08, 2010 12:57:08 PM

Correct. You will also want to be sure to update the title page at that time.

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 08, 2010 12:56 PM
To: Abel, Brendan
Subject: Re: Change of authorship

We will have a few additions to the acknowledgements. Our understanding is that these can be inserted once we get the galleys.

Thanks
Rose

From: Abel, Brendan <babel@nejm.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Mon Mar 08 12:01:42 2010
Subject: RE: Change of authorship

Perfect. So that is the only change? Brenda Morris will retain authorship on the oxygen saturation paper?

Thanks,
Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, March 08, 2010 11:56 AM
To: Abel, Brendan
Subject: RE: Change of authorship

Brendan
I have drafted and attached a letter – can you tell me if this will suffice with the appropriate signatures?
Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Monday, March 08, 2010 11:09 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Change of authorship

Dear Rose.

Journal policy dictates that we must receive a signed letter from each author (including any that have been added or removed), indicating awareness of and agreement with the new authorship list. We will

need a separate letter for each manuscript; however, multiple changes in authorship to a single manuscript can be indicated on one form.

It would be most efficient if all of the authors signed one letter. However, if this is not possible, the corresponding author may collect individual copies of the letter and fax them to us in a collated batch. Please fax the letter to my attention at 781-207-6529 as soon as possible.

You will find a suggestion for the text of the letter below. As indicated, you are welcome to combine the language to cover an author deletion and addition for one manuscript on the same form. However, if the deleted author is then added to a different manuscript, we'll need a separate form that that addition.

I'll be around my desk for most of today. Certainly from now until 12:30, and then from 2-4:30. Feel free to call me with any questions.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

SUGGESTED TEXT FOR A NEW AUTHOR:

I, the undersigned, am aware of and agree with the addition of [INSERT NEW AUTHOR NAME(S)] to the manuscript submitted to the New England Journal of Medicine, "Manuscript title" (Manuscript ID #).

(The following should be the complete new author list in the order in which the names appear in the manuscript.)

AUTHOR NAME
AUTHOR NAME
AUTHOR NAME
AUTHOR NAME

Signed: _____ Date: _____

Print Name: _____

SUGGESTED TEXT FOR A DELETED AUTHOR:

I, the undersigned, am aware of and agree with the deletion of [INSERT DELETED AUTHOR NAME(S)] from the manuscript submitted to the New England Journal of Medicine, "Early CPAP versus Surfactant in Extremely Preterm Infants" (09-11783.R3).

(The following should be the complete new author list in the order in which the names appear in the manuscript.)

AUTHOR NAME
AUTHOR NAME
AUTHOR NAME
AUTHOR NAME

Signed: _____ Date: _____

Print Name: _____

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From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: re: change of authorship
Date: Monday, March 08, 2010 9:53:51 AM

Hi Rose,

Thanks for your note. I actually think it will be easier for me to explain the change of author process by email. I have a meeting from 10-11 this morning, but I should be able to get back to you after that. You can then of course call with any follow-up questions.

Thanks,

Brendan

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Editorial Assistant
New England Journal of Medicine
(617) 487-6584

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From: Kurt Schibler
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: ****Important NEJM acknowledgements*****
Date: Monday, March 08, 2010 9:09:47 AM

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Thanks,
Kurt

Kurt Schibler, MD
Associate Professor of Pediatrics
Division of Neonatology, ML 7009
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, Ohio 45229
TEL: 513-636-3972
Pager: 513-736-5649
E-mail: kurt.schibler@cchmc.org

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higginsr@mail.nih.gov

From: [Barbara Stoll](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: ****Important NEJM acknowledgements*****
Date: Friday, March 05, 2010 10:28:23 PM

boilerplate looks AOK to me
THANKS

Barbara J. Stoll, MD
George W. Brumley, Jr., Professor and Chair, Department of Pediatrics
Chief Academic Officer, Children's Healthcare of Atlanta
President and CEO, Emory-Children's Center
2015 Uppergate Dr
Atlanta GA 30022
Office: 404-727-2456 Fax: 404-727-5737
barbara_stoll@oz.ped.emory.edu

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From: Walsh, Michele
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ****Important NEJM acknowledgements*****
Date: Friday, March 05, 2010 11:54:00 AM

Ours are correct.

Michele Walsh
beeper 30642
Ph 216 844 3759

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 9:18 AM
To: 'Finer, Neil'; 'Duara, Shahnaz'; Phelps, Dale; 'Michael O`Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: 'Zaterka-Baxter, Kristin'
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From: Edward Donovan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: ****Important NEJM acknowledgements*****
Date: Friday, March 05, 2010 10:25:01 AM

Both OK by me.

Edward F. Donovan, M.D.
Ohio Perinatal Quality Collaborative
www.OPQC.net

Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0169
Fax 513-636-0171
www.cincinnatichildrens.org/cprc

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 3/5/2010 9:17 AM >>>

Hi,

It was brought to our attention that at least one site has a staff member missing on the acknowledgements section of the SUPPORT papers. I spoke with Brendan Abel, editorial assistant at NEJM this morning and we will be permitted to insert additional names into the acknowledgements section. He pointed out that no changes can be made to the manuscript without the approval of the editor so the attached papers are final.

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The acknowledgements begin on page 20 for the CPAP/surf paper and on page 21 for the oxygen saturation paper.

Thanks for all your help and remember to keep the manuscripts confidential as NEJM has a very strict embargo policy.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Friday, March 05, 2010 10:20 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wally Carlo, M.D.
Subject: RE: ****Important NEJM acknowledgements*****

Thanks Rose
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 6:18 AM
To: Finer, Neil; 'Duara, Shahnaz'; Phelps, Dale; 'Michael O` Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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higginsr@mail.nih.gov

From: Frantz, Ivan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ****Important NEJM acknowledgements*****
Date: Friday, March 05, 2010 9:26:18 AM

Tufts is ok. MacKinnon should probably be listed second on the Carlo manuscript, but this is not essential.

Ivan D. Frantz, III, M.D.
Professor of Pediatrics
Tufts University School of Medicine

Tufts Medical Center Box 44
800 Washington St.
Boston, MA 02111

617 636 5322

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 9:18 AM
To: 'Finer, Neil'; 'Duara, Shahnaz'; Phelps, Dale; 'Michael O`Shea'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Frantz, Ivan; Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLdberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"; "Wally Carlo, M.D."
Subject: FW: ****Important NEJM acknowledgements*****
Date: Friday, March 05, 2010 9:25:00 AM

I spoke to Brendan – we can insert names when you get the galleys. I will get the sites responses and generate a list for each of you.
Brendan was very receptive to this request!!!

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, March 05, 2010 9:18 AM
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Higgins, Rosemary (NIH/NICHD) [E]

From: Michael O`Shea <moshea@wfubmc.edu>
Sent: Friday, March 05, 2010 9:21 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ****Important NEJM acknowledgements*****

Rose,
The information for Wake Forest is correct
Thank you
Mike

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, March 05, 2010 9:18 AM
To: 'Finer, Neil'; 'Duara, Shahnaz'; Phelps, Dale; Michael O`Shea; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MIckey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
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From: Bock, Robert (NIH/NICHD) [E]
To: "Lila Guterman"; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release
Date: Thursday, March 04, 2010 4:40:43 PM

I was afraid I'd missed something.

From: Lila Guterman [mailto:lguterman@palladianpartners.com]
Sent: Thursday, March 04, 2010 4:37 PM
To: Bock, Robert (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

Yes!

From: Bock, Robert (NIH/NICHD) [E] [mailto:bockr@exchange.nih.gov]
Sent: Thursday, March 04, 2010 4:16 PM
To: 'Lila Guterman'; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

You mean on the 11th, right?

From: Lila Guterman [mailto:lguterman@palladianpartners.com]
Sent: Thursday, March 04, 2010 4:04 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

Great! Let's say 1 p.m. on the 1st.

Quick question before then – do you know when NEJM is planning to publish the paper(s)? Will they appear together?

Thanks!

Lila

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, March 04, 2010 4:01 PM
To: 'Lila Guterman'
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

12-2 on the 11th still works for me

Rose

From: Lila Guterman [mailto:lguterman@palladianpartners.com]
Sent: Thursday, March 04, 2010 3:56 PM

To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

The 11th would work better for me. I can do 8:30 or 9 a.m. or anytime between 12 and 2.

Thanks!

Lila

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, March 03, 2010 3:01 PM
To: 'Lila Guterman'
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

March 9 1-4 PM or anytime on March 11
Thanks and I look forward to it!
Rose

From: Lila Guterman [mailto:lguterman@palladianpartners.com]
Sent: Wednesday, March 03, 2010 2:57 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: Interview request for NICHD press release

Dear Dr. Higgins,

I am a science writer working with Bob Bock to write press releases. We would like to set up a time to talk with you about the SUPPORT paper that will appear in the New England Journal of Medicine. Is there a time next week when we could set up a phone call?

Thank you very much,

Lila Guterman

Lila Guterman
Senior Writer
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Phone: 301.650.8660 (M, W) 202.232.2837 (T, Th, Fri)
lguterman@palladianpartners.com

From: [Spong, Catherine \(NIH/NICHD\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: NRN PAS presentation and upcoming publications in NEJM
Date: Thursday, March 04, 2010 4:28:04 PM

Congratulations and stellar work!

Catherine Y Spong MD
Chief, Pregnancy and Perinatology Branch
Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health
6100 Executive Blvd, Rm 4B03, MSC 7510
Bethesda MD 20892 (express mail: Rockville MD 20852)
Phone 301 435 6894 or 301 496 5575
Fax 301 496 3790
email spong@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Sent: Thursday, March 04, 2010 3:46 PM
To: [Guttmacher, Alan \(NIH/NICHD\) \[E\]](#); [Maddox, Yvonne \(NIH/NICHD\) \[E\]](#); [Hanson, James \(NIH/NICHD\) \[E\]](#); [Hewitt, Tyl \(NIH/NICHD\) \[E\]](#)
Cc: [Spong, Catherine \(NIH/NICHD\) \[E\]](#); [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Subject: NRN PAS presentation and upcoming publications in NEJM

Hi,

I have attached the presentation schedule for the NICHD Neonatal Research Network for the Pediatric Academic Societies meeting May 1-4, 2010 in Vancouver. We have 19 abstracts which were accepted for presentation (8 platforms and 11 posters). This year, we have also included the Hot Topic, Topic Symposium, State of the Art Plenary, and Clubs that our network investigators have been asked to speak based on NRN studies, publications, and structure.

We had both of our primary papers from the SUPPORT (The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight (ELBW) Infants) Trial accepted for publication in the New England Journal (no date yet for publication). This is a very large study of 1316 infants to compare CPAP (continuous positive airway pressure) with surfactant and intubation; and two different levels of targeted oxygen saturation. The study was co-funded by the Lung Division at NHLBI. Both studies are being presented as platforms at PAS and are highly likely to impact medical practice and care of ELBW infants. NHLBI has requested that the SUPPORT results also be presented in a designated NHLBI session at the American Thoracic Society meeting in May 2010. I am working with Bob Bock for press issues.

The conclusion from the CPAP/surfactant paper is:

These results support consideration of CPAP as an alternative to intubation and surfactant in preterm infants.

The conclusions from the saturation paper are:

A lower (85 to 89%), as compared with a higher (91 to 95%) oxygen saturation target did not significantly decrease the combined outcome of severe retinopathy or death but resulted in an increase in mortality and a substantial decrease in severe retinopathy among survivors. The increase in mortality is a major concern as lower

saturation targeting is increasingly being advocated to prevent retinopathy of prematurity.

Thank you for the continued support for the NRN.

Best regards,

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

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From: Bock, Robert (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]; "Lila Guterman"
Subject: RE: Interview request for NICHD press release
Date: Thursday, March 04, 2010 4:17:06 PM

Really? Now that's really something.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thursday, March 04, 2010 4:17 PM
To: 'Lila Guterman'
Cc: Bock, Robert (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release

1 PM on the 11th. We do not have a publication date. The implication from NEJM was that both would appear in the same issue

Rose

From: Lila Guterman [mailto:lguterman@palladianpartners.com]
Sent: Thursday, March 04, 2010 4:04 PM
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Sent: Wednesday, March 03, 2010 3:01 PM

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Subject: RE: Interview request for NICHD press release

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Lila Guterman

Senior Writer

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lguterman@palladianpartners.com

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Das, Abhik"; "Wallace, Dennis"
Subject: study time lines
Date: Thursday, March 04, 2010 3:59:00 PM

Hi,

I have to give two upcoming talks on the NRN with respect to the hypothermia studies and the SUPPORT trial. The hypothermia talk is in a "clinical trials for neuroprotection" topic symposium at PAS and the SUPPORT talk is a brief introduction of the SUPORT trial in the NRN for the American Thoracic Society meeting in mid-may.

I am wondering if someone from the DCC can help me with **the timelines** for the studies.

I envision a powerpoint slide(s) for SUPPORT with the DR CPAP pilot, protocol development, protocol training (9/2004), study recruitment (Feb 2005-Nov 2005, pause, restart Feb 2006-Feb 2009).

For hypothermia:

Original trial – same timeline as above + FU and school age FU

I also plan to mention the 6-24 hour study and the upcoming optimizing cooling trial. Is it possible that someone could help?? Marie for SUPPORT and Scott for hypothermia?? Or perhaps Carolyn?? Let me know

Rosemary D. Higgins, MD
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To: "Lila Guterman"; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Interview request for NICHD press release
Date: Thursday, March 04, 2010 3:57:25 PM

It would need to be afternoon for me.

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Sent: Thursday, March 04, 2010 3:56 PM
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Cc: Bock, Robert (NIH/NICHD) [E]
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Lila Guterman

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Senior Writer

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Phone: 301.650.8660 (M, W) 202.232.2837 (T, Th, Fri)

lguterman@palladianpartners.com

From: Das, Abhik
To: Higgins, Rosemary (NIH/NICHD) [E]; Wallace, Dennis
Subject: RE: THANKS
Date: Thursday, March 04, 2010 12:14:04 AM

Thank you. Dennis can inform the staff concerned. Meanwhile I am rejoicing in the twin SUPPORT acceptances -- this is historic for the NRN!

Abhik

Abhik Das
Senior Research Statistician
RTI International

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, March 03, 2010 04:23 PM Eastern Standard Time
To: Das, Abhik; Wallace, Dennis
Subject: THANKS

Abhik and Dennis

This email is long overdue. I want to sincerely thank the efforts of RTI, especially Meg Cunningham, Kris Baxter, James Pickett, and Carolyn Huitema for the last minute change of the Steering Committee meeting from the Bolger Venue to the phone conference on February 11-12 due to the snow storm. The RTI staff were professional, terrific, helpful and pleasant. They also did this on a moments notice and with such ease!!!!.

I have sent out a request for feedback on this last minute phone meeting and will certainly share all the results with you - most of the folks miss the interaction and thought the web slides were very useful.

Again thanks to you and your staff!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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Eunice Kennedy Shriver National Institute of Child Health and Human Development
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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT papers to SC
Date: Wednesday, March 03, 2010 12:41:18 PM

I usually do.

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, March 03, 2010 12:38 PM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT papers to SC

11/6 –

You should log these in as they go to the steering committee

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, March 03, 2010 11:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT papers to SC

Since I know you just looked this up, when did Wally's and Neil's papers get sent to the SC? Just need to enter a date in the tracker.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: SUPPORT papers to SC
Date: Wednesday, March 03, 2010 12:38:00 PM
Attachments: CONFIDENTIAL_SUPPORT_DRAFT_MANUSCRIPTS.htm

11/6 –

You should log these in as they go to the steering committee

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Wednesday, March 03, 2010 11:34 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT papers to SC

Since I know you just looked this up, when did Wally's and Neil's papers get sent to the SC? Just need to enter a date in the tracker.

From: Higgins, Rosemary (NIH/NICHD) [E]

Sent: Friday, November 06, 2009 4:42 PM

To: nfiner@ucsd.edu; 'wrich@ucsd.edu'; Gantz, Marie; 'Nancy Newman'; 'Susie Buchter'; 'Brenda Morris'; 'Laroia, Nirupama'; Sood, Beena; sduara@miami.edu; 'Michael O`Shea'; Anthony Piazza; vineet.bhandari@yale.edu; 'Vivek.Narendran@cchmc.org'; Phelps, Dale; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa

Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; Cunningham, Meg; Huitema, Carolyn Petrie

Subject: ****CONFIDENTIAL SUPPORT DRAFT MANUSCRIPTS*****

Attachments: Tables Nov 3 09.docx; Oxygen Saturation Target 11 6 09 MASTER (2).doc; SUPPORT CPAP vs Surf Nov 3 09 doc for circ (2).docx

Hi,

Attached are the two papers in draft form for the SUPPORT Primary outcomes. As noted, there is an increase in death in the lower saturation group (20%) versus the higher saturation group (16%).

This information is confidential and a plan is in place for DSMC communication with ongoing trials of oxygen saturation. If you are contacted by any investigators from other trials or elsewhere, do not share this information. If necessary, refer them to me.

The plan for submission is as follows:

November 16 – 4 PM – call for Steering committee and authors to discuss papers.

In the meantime, feel free to send comments to Neil and Wally. The call in number is: 866-675-3256 with passcode 560152#

If you are not going to be on the call, send comments in advance or designate someone to serve in your absence.

Immediately following the call, the manuscripts will be finalized for NICHD clearance and for submission to the New England Journal of Medicine.

Thanks in advance to everyone for all their hard work!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Poe, Grace \(NIH/NICHD\) \[E\]](#)
Cc: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Subject: SUPPORT MRI Follow Up
Date: Tuesday, March 02, 2010 9:40:00 AM

Extended Follow-up at School Age (6½ to 7½ years) for the SUPPORT Neuroimaging and Neurodevelopmental Outcomes Cohort

The SUPPORT Neuroimaging cohort is valuable and unique among other preterm cohorts worldwide. By pursuing 6½ - 7½ year follow-up, the NICHD NRN is in an outstanding position to substantially contribute to our understanding of later extremely preterm outcomes and their prediction.

Recruitment into the SUPPORT Trial spanned from 2004 through February 2009. IN order to follow these children through school age, the study will extend through 2016. There are 558 children who are in this secondary study to the main SUPPORT Trial.

Let me know if you need more information

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Kristi Watterberg"
Subject: RE: Fwd: ICMJE's for SUPPORT papers
Date: Monday, March 01, 2010 11:04:00 AM

THANKS
ROSE

From: Kristi Watterberg [mailto:KWatterberg@salud.unm.edu]
Sent: Monday, March 01, 2010 10:53 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: Fwd: ICMJE's for SUPPORT papers

it looks like they use the latest version of Adobe, so I couldn't see some of the boxes. I understand you talked with Heather, who will revise and re-send. Sorry for the glitch! I will find out how much it costs to update Acrobat and get it done ~ Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/27/2010 8:38 AM >>>
Brendan will send me a list on Monday - he still had you on the list when I spoke to Heather yesterday. If you need to do anything else, I will let you know

Thanks (and sorry for the trouble)

Rose

----- Original Message -----

From: Kristi Watterberg <kwatterberg@salud.unm.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Sat Feb 27 10:06:38 2010
Subject: Fwd: ICMJE's for SUPPORT papers

Rose, we did fill out on computer, save and e-mail, as you will see from the forwarded email. Could it be that he needs it sent from my personal email? We weren't notified of that - got no response that I know of. Kristi

Blansfield, Earl (NIH/NICHD) [E]

From: Abel, Brendan <babel@nejm.org>
Sent: Monday, March 01, 2010 10:53 AM
To: 'Heather Shinn'; Brendan 'Abel' <babel@nejm.org>
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE forms

Hi Heather,

Thanks for sending. Dr. Watterberg is now all set.

Brendan

-----Original Message-----

From: Heather Shinn [<mailto:HShinn@salud.unm.edu>]
Sent: Monday, March 01, 2010 10:21 AM
To: Brendan 'Abel' <babel@nejm.org>
Cc: higginsr@mail.nih.gov
Subject: ICMJE forms

Brendan,
The forms for Kristi Watterberg are edited and attached.
If you have any questions, please let me know.
Thank you.
-Heather

Heather Shinn
Admin Asst III to:
-Dr. Kristi Watterberg
-Dr. Andrea Duncan
-Dr. Erika Fernandez
Dept of Pediatrics/Neonatology
ACC-3 West
2211 Lomas Blvd NE
Albuquerque, NM 87131
(505) 272-0180

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: [Edward Donovan](#)
To: babel@nejm.org
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: New England Journal of Medicine 09-11783.R2
Date: Monday, March 01, 2010 9:29:42 AM
Attachments: [Donovan-ICMJE-Disclosure-form Donovan.pdf](#)

attached

Edward F. Donovan, M.D.
Ohio Perinatal Quality Collaborative
www.OPQC.net

Child Policy Research Center
Children's Hospital Medical Center
3333 Burnet Avenue, ML 7014
Cincinnati, OH 45229-3039
Phone 513-636-0169
Fax 513-636-0171
www.cincinnatichildrens.org/cprc

>>> <babel@nejm.org> 3/1/2010 8:54 AM >>>

Re: 09-11783.R2 - Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Dear Dr. Donovan:

Please fill out and return the attached ICMJE disclosure form to me via email at your soonest convenience. We will not be able to proceed with sending the above manuscript to the editor in chief until we have received your form.

Feel free to contact me with any questions.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:

(or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
 Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD Neonatal Research Network		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD Neonatal Research Network		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD Neonatal Research Network		Del ×
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del ×
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del ×" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

Tel. 301-496-0430

Fax 301-496-3790

archerst@mail.nih.gov<<mailto:archerst@mail.nih.gov>>

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Sunday, February 28, 2010 10:02 PM
To: Solomon, Caren, M.D.
Cc: Rich, Wade; Wally Carlo, M.D.; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE:
Attachments: NEJM Final Revision Tables and Figure Mar 1 Upload.doc; SUPPORT NEJM Revision Mar 1 Editor comments and responses .doc; SUPPORT NEJM Revision Mar 1 Upload .doc; SUPPORT NEJM Revision with edits and responses Mar 1 .doc

Hello Caren

Many thanks for your detailed review of our manuscript I have responded to each of your comments and made appropriate responses within the comment box and then in the manuscript We have clearly indicated that the Physiologic Definition of BPD is the Primary We should have done a protocol revision when we realized that we had not clearly also specified BPD by the classic definition, but we did not.

I have included only pre-specified outcomes in all Tables, and removed all others.

I added the outcome of duration of ventilation to the abstract and conclusion as this was a pre-specified outcome I moved the discussion of the number of tests and significance from the Methods to the Discussion where you indicated you thought these should go.

I added the words cross over to the Discussion when talking about the protocol design I have expanded on the definition of the physiologic definition with a brief line in the Abstract, more detail in the Methods, and Discussion For your review I am attaching a version in which all changes have been accepted with your comments and my responses shown. I have also attached a version with all relevant edits and comments shown, the revised Tables and Figure, and finally I have attached the Uploaded version for your review.

I appreciate your attention to our study, and I hope that the upload version is now acceptable for the Journal.

Be well

Neil

-----Original Message-----

From: Solomon, Caren, M.D. [mailto:csolomon@nejm.org]

Sent: Friday, February 26, 2010 2:25 PM

To: Finer, Neil

Cc: Rich, Wade

Subject: RE:

Neil and Wade,

Attached is an "almost final" version with remaining queries. On review of the protocol, appears that your prespecified primary outcome involved BPD using specifically the physiologic definition, and thus I re-edited abstract and methods to clarify.. (As I note in inserted comments, if this changes subsequently, please clarify..) Also I am asking that you be clear in your Table of secondary outcomes which were prespecified versus "other".. Otherwise, I have only a small number of relatively minor questions.

I look forward to seeing your manuscript back soon (Monday if possible) and will plan to move it promptly along.

Thanks again.

Caren

-----Original Message-----

From: Finer, Neil [mailto:nfiner@ucsd.edu]

Sent: Friday, February 26, 2010 2:46 PM
To: Solomon, Caren, M.D.
Cc: Rich, Wade
Subject: Re:

Hello Dr Solomon

I am in Ireland and for some reason I cannot attach the protocol here from my phone I sent the protocol from my laptop which did not get this message so I sent it to Brendan as I have his email there and not yours Please let me know if you receive the protocol Regards Neil finer

Sent from my iPhone

On Feb 25, 2010, at 3:14 AM, "Solomon, Caren, M.D." <csolomon@nejm.org<mailto:csolomon@nejm.org>> wrote:

Dear Dr. Finer,

Thanks for returning your manuscript so promptly.

I am in process of going back over it and will let you know any remaining questions in next day or so. But in the meantime, might I ask you to e-mail me copy of the study protocol? We generally ask for this in letter inviting revision, but we do not seem to have it...

Thanks in advance, and thanks again for your work.

Caren Solomon

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

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From: [Kristi Watterberg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: Fwd: ICMJE's for SUPPORT papers
Date: Saturday, February 27, 2010 11:39:06 AM

Thanks, Rose, let me know - I just want to get it right! Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/27/2010 8:38 AM >>>
Brendan will send me a list on Monday - he still had you on the list when I spoke to Heather yesterday. If you need to do anything else, I will let you know

Thanks (and sorry for the trouble)

Rose

----- Original Message -----

From: Kristi Watterberg <kwatterberg@salud.unm.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Sat Feb 27 10:06:38 2010
Subject: Fwd: ICMJE's for SUPPORT papers

Rose, we did fill out on computer, save and e-mail, as you will see from the forwarded email. Could it be that he needs it sent from my personal email? We weren't notified of that - got no response that I know of. Kristi

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "kwatterberg@salud.unm.edu"
Subject: Re: URGENT:FW: ICMJE's for SUPPORT papers
Date: Saturday, February 27, 2010 9:23:49 AM

They have to be filled out on a computer, saved and sent via email.

Sorry for the trouble

Rose

From: Kristi Watterberg <kwatterberg@salud.unm.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Sat Feb 27 08:38:10 2010
Subject: Re: URGENT:FW: ICMJE's for SUPPORT papers

Rose I sent both of those in the day you sent them. Did he not receive them? Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/26/2010 7:49 AM >>>
Your form is needed for the CPAP paper. Please fill it in and email it to Brendan Abel
(babel@nejm.org<mailto:babel@nejm.org>) TODAY!!

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Eunice Kennedy Shriver NICHD Neonatal Research Network
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301-496-3790 (FAX)
higginsr@mail.nih.gov<mailto:higginsr@mail.nih.gov>

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, February 24, 2010 12:04 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; 'Michael O'Shea'; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
Subject: ICMJE's for SUPPORT papers

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. Please do this today or tomorrow.

Thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abel, Brendan"
Subject: RE: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 4:40:00 PM

I just spoke to Dr. Van Meurs - she will have her forms in over the weekend or first thing Monday morning. She is offsite at a research retreat today. Ian Gross from Yale took care of Dr. Ehrenkranz's forms.

Let me know if anything else is missing and I can get in touch with folk. Thanks for your patience

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Abel, Brendan [<mailto:babel@nejm.org>]
Sent: Friday, February 26, 2010 4:15 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers

Hi Rose,

They are working. It's just the nature of the forms that leads to all of these issues (they're not intuitive, to say the least). We're working on it.

In the meantime, I called Heather and clarified that issue. Dr. Watterberg's forms will be in by Monday AM.

Brendan

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, February 26, 2010 4:09 PM
To: Abel, Brendan
Subject: FW: ICMJE's for SUPPORT papers

Brendan-

Are the forms I sent out earlier working?

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Heather Shinn [<mailto:HShinn@salud.unm.edu>]
Sent: Friday, February 26, 2010 4:07 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Brendan 'Abel' <babel@nejm.org>
Subject: Re: ICMJE's for SUPPORT papers

Rose,

These forms look exactly like the first two I filled out and sent to Brendan previously.

Where should I look to make sure it is the web based form so we don't have to fill them out again?

Thank you.

-Heather

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>

>>> 2/26/2010 2:03 PM >>>

Here are the forms. Please fill them in and email them back to Brendan Abel
(babel@nejm.org<<mailto:babel@nejm.org>>)

THANKS

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network _____ Rose Rosemary D.
Higgins, MD Program Scientist for the Neonatal Research Network Pregnancy and Perinatology Branch Center for
Developmental Biology and Perinatal Medicine Eunice Kennedy Shriver National Institute of Child Health and
Human Development National Institutes of Health 6100 Executive Blvd., Room 4B03 MSC 7510 Bethesda, MD
20892 For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

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Blansfield, Earl (NIH/NICHD) [E]

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, February 26, 2010 4:23 PM
To: 'Heather Shinn'; 'Brendan' 'Abel <babel@nejm.org>
Subject: RE: ICMJE's for SUPPORT papers

Brendan told me that these forms are working today.

You can fill it in, save it and email it to him

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Heather Shinn [<mailto:HShinn@salud.unm.edu>]
Sent: Friday, February 26, 2010 4:07 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Brendan' 'Abel <babel@nejm.org>
Subject: Re: ICMJE's for SUPPORT papers

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(babel@nejm.org<<mailto:babel@nejm.org>>)

THANKS

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network _____ Rose Rosemary D. Higgins,
MD Program Scientist for the Neonatal Research Network Pregnancy and Perinatology Branch Center for Developmental
Biology and Perinatal Medicine Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "hshinn@salud.unm.edu"
Subject: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 4:03:00 PM
Attachments: [ICMJE CPAP paper.pdf](#)
[ICMJE sat paper.pdf](#)
Importance: High

Here are the forms. Please fill them in and email them back to Brendan Abel (babel@nejm.org)

THANKS

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
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Manuscript Identifying Number (if you know it):

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

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Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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- Yes, the following relationships/conditions/circumstances are present (explain below):

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						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: ["babel@neim.org"](mailto:babel@neim.org)
Cc: ["Finer, Neil"](#); ["Wally Carlo, M.D."](#)
Subject: FW: Copyright form for Manuscript 09-11781
Date: Friday, February 26, 2010 3:41:00 PM
Attachments: [Neil Finer - Copyright form - 09-11781.pdf](#)
[Neil Finer - ICMJE Disclosure Form - 09-11781.pdf](#)

Brendan

I think most folks have responded. I haven't heard from Drs. Ehrenkranz, Watterberg, or Van Meurs. Have these investigators sent in their forms??

thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Martinez, Fernando [<mailto:fmartinez@ucsd.edu>]
Sent: Friday, February 26, 2010 3:34 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Finer, Neil
Subject: Copyright form for Manuscript 09-11781

Dear Dr. Higgins,

On behalf of Dr. Finer, please find attached his signed copyright form for manuscript 09-11781 (Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial). In addition, I've attached his completed disclosure form. I will also send both documents to the journal.

Please don't hesitate to contact me if you have questions or need additional information.

Kind regards,

Fernando I. Martinez
Administrative Supervisor
Assistant to Division Director, Dr. Neil N. Finer
UC San Diego School of Medicine
UC San Diego Medical Center, Hillcrest
Department of Pediatrics
Division of Neonatal-Perinatal Medicine
402 Dickinson St., MPF 1-140
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Short Title or description of Contribution: Oxygen Saturation Targets in Extremely Preterm

Corresponding Author: Infants: The Support Trial

Wally Carlo, M.D.

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Neil N.

Surname:
(or last)

Finer

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26-February-2010

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Corresponding author's name:

Wally Carlo, M.D.

Manuscript Title:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

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Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Michele.Walsh@UHhospitals.org"
Subject: Re: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 12:49:27 PM

617-734-9800

From: Walsh, Michele <Michele.Walsh@UHhospitals.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Feb 26 12:45:11 2010
Subject: Re: ICMJE's for SUPPORT papers

I sent it in twice already will try again what is Brendan phone no.

----- Original Message -----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
To: mcw3@cwru.edu <mcw3@cwru.edu>
Sent: Fri Feb 26 09:57:14 2010
Subject: FW: ICMJE's for SUPPORT papers

Michele

Brendan tells us that you are missing a checked box in the consulting fee row in section 2 for teh CPAP paper. Can you send this to him TODAY at babel@nejm.org <<mailto:babel@nejm.org>>?

thanks

ROse

Rosemary D. Higgins, MD
Program Scientist for the Eunice Kennedy Shriver NICHD Neonatal Research Network
Pregnancy and Perinatology Branch
CDBPM, NIH
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20592
301-435-7909
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov <<mailto:higginsr@mail.nih.gov>>

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, February 26, 2010 9:50 AM
To: 'ambal@uab.edu'
Cc: 'wcarlo@peds.uab.edu'
Subject: Fw: ICMJE's for SUPPORT papers

Ambal

Please email these to Brendan Abel (babel@nejm.org)

Thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'Duara, Shahnaz' <SDuara@med.miami.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>;

kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; Bell, Edward <edward-bell@uiowa.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; nancy newman <nxs5@case.edu>; 'Michael O'Shea' <moshea@wfubmc.edu>; 'Poindexter, Brenda B' <bpoindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:04:45 2010
Subject: ICMJE's for SUPPORT papers

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. Please do this today or tomorrow.

Thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

Visit us at www.UHhospitals.org.

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Federal and Ohio law protect patient medical information, including psychiatric_disorders, (H.I.V) test results, A.I.Ds-related conditions, alcohol, and/or drug_dependence or abuse disclosed in this email. Federal regulation (42 CFR Part 2) and Ohio Revised Code section 5122.31 and 3701.243 prohibit disclosure of this information without the specific written consent of the person to whom it pertains, or as otherwise permitted by law.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "NAmbalavanan@peds.uab.edu"
Subject: Re: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 10:42:10 AM

Thanks
Rose

From: Namasivayam Ambalavanan <NAmbalavanan@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; ambal@uab.edu <ambal@uab.edu>; babel@nejm.org <babel@nejm.org>
Cc: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
Sent: Fri Feb 26 10:38:01 2010
Subject: RE: ICMJE's for SUPPORT papers

Dear Mr Brendan Abel,
Attached are the two ICMJE forms.
Thank you,
Ambalavanan

N. Ambalavanan MD
Associate Professor, Division of Neonatology
Departments of Pediatrics, Cell Biology, and Pathology

Mailing Address:
176F Suite 9380
619 South 19th Street
Birmingham, AL 35249-7335
Tel Office (205) 934 4680 Lab (205) 934 0751 or 996 5419
Fax Office (205) 934-3100 Lab (205) 996 2333
Email ambal@uab.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Fri 2/26/2010 8:50 AM
To: 'ambal@uab.edu'
Cc: Wally Carlo, M.D.
Subject: Fw: ICMJE's for SUPPORT papers

Ambal
Please email these to Brendan Abel (babel@nejm.org)

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'Duara, Shahnaz' <SDuara@med.miami.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; Bell, Edward <edward-bell@uiowa.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; nancy newman <nxs5@case.edu>; 'Michael O`Shea' <moshea@wfubmc.edu>; 'Poindexter, Brenda B' <bpoindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan' <babel@nejm.org>

Sent: Wed Feb 24 12:04:45 2010

Subject: ICMJE's for SUPPORT papers

Hi,

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Thanks for all your help

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institutes of Health

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Karen Kirby
To: babel@nejm.org
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#); [Karen Kirby](#); [Pablo Sanchez](#)
Subject: Fwd: URGENT REQUEST:: SUPPORT forms
Date: Friday, February 26, 2010 10:28:07 AM
Attachments: [ICMJE saturation paper.pdf](#)
[ICMJE CPAP vs Surfactant paper.pdf](#)

Brendan,
I am attaching both ICMJE Uniform Disclosure Forms for Dr. Pablo Sánchez.
Please let me know if you need additional information.
Thank you.
Karen Kirby for Pablo Sánchez

Hi,
Brendan is missing your form for the saturation paper - please submit the fillable form (attached) and email it to Him today at babel@nejm.org.

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; Vivek Narendran <Vivek.Narendran@cchmc.org>; Phelps, Dale <Dale_Phelps@URMC.Rochester.edu>; Anthony Piazza <Anthony.Piazza@oz.ped.emory.edu> <Anthony.Piazza@oz.ped.emory.edu>
Cc: 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:11:30 2010
Subject: SUPPORT forms

Hi all,
Please fill out the attached form, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help!
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Pablo

Surname:
(or last)

Sanchez

Effective Date:

30-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar Carlo, MD

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHHD	U10HD40689	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHHD	U10HD40689	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
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						Add +
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						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

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Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	U10HD40689	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	U10HD40689	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo.Sanchez@UTSouthwestern.edu"
Subject: Re: URGENT REQUEST:: SUPPORT forms
Date: Friday, February 26, 2010 10:14:10 AM

Thanks

----- Original Message -----

From: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Feb 26 10:13:06 2010
Subject: Re: URGENT REQUEST:: SUPPORT forms

OK--I think what happened is that we fax'd them to the office and they want electronic versions and not paper copy-
---pablo

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/26/10 9:01 AM >>>

Ok

Thanks - brendan had sent me a "missing" list today and for some reason, he was still missing both ICMJE's (one for each paper) from you.

Thanks

Rose

----- Original Message -----

From: Pablo Sanchez <Pablo.Sanchez@UTSouthwestern.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Feb 26 09:58:20 2010
Subject: Re: URGENT REQUEST:: SUPPORT forms

ok, but I had done it, will redo---pablo

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/26/10 8:32 AM >>>

Hi,

Brendan is missing your form for the saturation paper - please submit the fillable form (attached) and email it to Him today at babel@nejm.org.

Thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; Vivek Narendran <Vivek.Narendran@cchmc.org>; Phelps, Dale <Dale_Phelps@URMC.Rochester.edu>; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu) <Anthony.Piazza@oz.ped.emory.edu>
Cc: 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:11:30 2010
Subject: SUPPORT forms

Hi all,

Please fill out the attached form, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. Please do this today or tomorrow.

Thanks for all your help!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Abel, Brendan
To: "Vineet Bhandari"
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICJME form for CPAP mans # 09-11783
Date: Friday, February 26, 2010 10:13:13 AM

Great. You're all set.

Thanks,

Brendan

From: Vineet Bhandari [mailto:vineet.bhandari@yale.edu]
Sent: Friday, February 26, 2010 10:10 AM
To: Abel, Brendan
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: ICJME form for CPAP mans # 09-11783
Importance: High

Hello, Brendan,

Please find attached the completed ICJME form, as requested.

Thank you.

Best wishes.
Vineet.

Vineet Bhandari, MD, DM
Associate Professor
Yale University School of Medicine
Division of Perinatal Medicine
Department of Pediatrics
Children's Hospital LCI 401B
P.O. Box 208064
333 Cedar Street
New Haven, CT 06520-8064
Phone: 203-785-2613
Fax: 203-785-6974

Email Disclaimer:

Please be aware that email communication can be intercepted in transmission or misdirected. Your use of email to communicate protected health information to us indicates you acknowledge and accept the possible risks associated with such communication. Please consider communicating any sensitive information by telephone, fax or mail. If you do not wish to have your information sent by email, please contact the sender immediately. The information contained in this message may be Privileged and Confidential. If you are NOT the intended recipient, please notify the sender immediately with a copy to hipaa.security@yale.edu and destroy this message.

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "NAmbalayanan@peds.uab.edu"; "ambal@uab.edu"
Cc: "wcarlo@peds.uab.edu"
Subject: Re: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 10:06:16 AM

These need to be emailed on the "fillable" form.

Thanks for your patience

Rose

----- Original Message -----

From: Namasivayam Ambalavanan <NAmbalayanan@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; ambal@uab.edu <ambal@uab.edu>
Cc: wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>
Sent: Fri Feb 26 10:05:38 2010
Subject: RE: ICMJE's for SUPPORT papers

Dear Dr. Higgins,

Sure - I had already faxed this form earlier but I will send them again by email.
Ambal

-----Original Message-----

From: "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
To: "ambal@uab.edu" <ambal@uab.edu>
Cc: "wcarlo@peds.uab.edu" <wcarlo@peds.uab.edu>
Sent: 2/26/2010 8:51 AM
Subject: Fw: ICMJE's for SUPPORT papers

Ambal

Please email these to Brendan Abel (babel@nejm.org)

Thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'Duara, Shahnaz' <SDuara@med.miami.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; Bell, Edward <edward-bell@uiowa.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; nancy newman <nxs5@case.edu>; 'Michael O' Shea' <moshea@wfubmc.edu>; 'Poindexter, Brenda B' <bpoindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:04:45 2010
Subject: ICMJE's for SUPPORT papers

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. Please do this today or tomorrow.

Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: mcw3@cwru.edu
Subject: FW: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 9:57:15 AM
Attachments: ICMJE CPAP paper.pdf
Importance: High

Michele

Brendan tells us that you are missing a checked box in the consulting fee row in section 2 for teh CPAP paper. Can you send this to him TODAY at babel@nejm.org?

thanks

ROse

Rosemary D. Higgins, MD

Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research Network

Pregnancy and Perinatology Branch

CDBPM, NIH

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20592

301-435-7909

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, February 26, 2010 9:50 AM
To: 'ambal@uab.edu'
Cc: 'wcarlo@peds.uab.edu'
Subject: Fw: ICMJE's for SUPPORT papers

Ambal

Please email these to Brendan Abel (babel@nejm.org)

Thanks

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'Duara, Shahnaz' <SDuara@med.miami.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; Bell, Edward <edward-bell@uiowa.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; nancy newman <nxs5@case.edu>; 'Michael O` Shea' <moshea@wfubmc.edu>; 'Poindexter, Brenda B' <bpindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:04:45 2010
Subject: ICMJE's for SUPPORT papers

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Rose

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ICMJE

INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Early CPAP versus Surfactant in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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MEDICAL JOURNAL EDITORS

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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "kzaterka@rti.org"
Subject: Re: URGENT REQUEST:: SUPPORT forms
Date: Friday, February 26, 2010 9:51:08 AM

Yes

Thanks
Rose

From: Zaterka-Baxter, Kristin <kzaterka@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Feb 26 09:49:07 2010
Subject: RE: URGENT REQUEST:: SUPPORT forms

Hi,

For Ken, Grants would be marked as yes , then NICHD as entity right? Sorry, still new at this.

Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 26, 2010 9:32 AM
To: 'richard.ehrenkranz@yale.edu'; Poole, W. Kenneth; 'ambal@uab.edu';
'Pablo.Sanchez@UTSouthwestern.edu'; 'vanmeurs@leland.stanford.edu'; 'kwatterberg@salud.unm.edu'
Cc: Zaterka-Baxter, Kristin
Subject: URGENT REQUEST:: SUPPORT forms

Hi,

Brendan is missing your form for the saturation paper - please submit the fillable form (attached) and email it to Him today at babel@nejm.org.

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; Vivek Narendran
<Vivek.Narendran@cchmc.org>; Phelps, Dale <Dale_Phelps@URMC.Rochester.edu>; Anthony Piazza
(Anthony.Piazza@oz.ped.emory.edu) <Anthony.Piazza@oz.ped.emory.edu>
Cc: 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:11:30 2010
Subject: SUPPORT forms

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Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "ambal@uab.edu"
Cc: "wcarlo@peds.uab.edu"
Subject: Fw: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 9:50:43 AM
Attachments: [ICMJE CPAP paper.pdf](#)
[ICMJE sat paper.pdf](#)
Importance: High

Ambal
Please email these to Brendan Abel (babel@nejm.org)

Thanks
Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: 'Duara, Shahnaz' <SDuara@med.miami.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; Bell, Edward <edward-bell@uiowa.edu>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; nancy newman <nxs5@case.edu>; 'Michael O`Shea' <moshea@wfubmc.edu>; 'Poindexter, Brenda B' <bpoindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:04:45 2010
Subject: ICMJE's for SUPPORT papers

Hi,
Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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For overnight delivery use Rockville, MD 20852
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301-496-3790 (FAX)
higginsr@mail.nih.gov



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Manuscript Identifying Number (if you know it):

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						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Format example: 07-August-2008

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Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

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Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: edward.donovan@cchmc.org; vineet.bhandari@yale.edu; kwatterberg@salud.unm.edu; Pablo.Sanchez@UTSouthwestern.edu; vanmeurs@stanford.edu; poo@rti.org
Cc: [\(kzaterka@rti.org\)](mailto:(kzaterka@rti.org))
Subject: URGENT:FW: ICMJE's for SUPPORT papers
Date: Friday, February 26, 2010 9:43:24 AM
Attachments: [ICMJE CPAP paper.pdf](#)
Importance: High

Your form is needed for the CPAP paper. Please fill it in and email it to Brendan Abel (babel@nejm.org) TODAY!!

Thanks

Rose

Rosemary D. Higgins, MD

Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research Network

Pregnancy and Perinatology Branch

CDBPM, NIH

6100 Executive Blvd., Room 4B03

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Bethesda, MD 20892

For overnight delivery use Rockville, MD 20592

301-435-7909

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wednesday, February 24, 2010 12:04 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; 'Michael O` Shea'; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
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To: "richard.ehrenkranz@yale.edu"; "poo@rti.org"; "ambal@uab.edu"; "Pablo.Sanchez@UTSouthwestern.edu"; "vanmeurs@leland.stanford.edu"; "kwatterberg@salud.unm.edu"
Cc: "kzaterka@rti.org"
Subject: URGENT REQUEST:: SUPPORT forms
Date: Friday, February 26, 2010 9:32:01 AM
Attachments: ICMJE sat paper.pdf

Hi,
Brendan is missing your form for the saturation paper - please submit the fillable form (attached) and email it to Him today at babel@nejm.org.

Thanks
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To: richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; Vivek Narendran <Vivek.Narendran@cchmc.org>; Phelps, Dale <Dale_Phelps@URMC.Rochester.edu>; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu) <Anthony.Piazza@oz.ped.emory.edu>
Cc: 'Abel, Brendan' <babel@nejm.org>
Sent: Wed Feb 24 12:11:30 2010
Subject: SUPPORT forms

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The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



ICMJE

INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Zaterka-Baxter, Kristin"
Subject: RE: SUPPORT ROP adjudication document summary
Date: Thursday, February 25, 2010 3:22:00 PM

That's it

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Thursday, February 25, 2010 3:21 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT ROP adjudication document summary

No bother at all – please see attached – let me know if these are the ones you need.

Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 25, 2010 3:19 PM
To: Zaterka-Baxter, Kristin
Subject: SUPPORT ROP adjudication document summary

Kris

Sorry to bother you but can you send me the summary document that Marie generated with respect to the ROP adjudication? I don't have access to all of my files.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Cunningham, Meg"
Subject: RE: author list SUPPORT abstracts
Date: Thursday, February 25, 2010 2:20:00 PM

Both went in with Neil and Wally on behalf of SUPPORT SUBCOMMITTEE

From: Cunningham, Meg [mailto:mcunningham@rti.org]
Sent: Thursday, February 25, 2010 2:15 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: author list SUPPORT abstracts

Are the authors for the two SUPPORT abstracts just Finer and Carlo on both?

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From: Abel, Brendan
To: "Zaterka-Baxter, Kristin"; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]; Das, Abhik
Subject: RE: Saturation paper and copyright form
Date: Thursday, February 25, 2010 9:30:20 AM

Hi Kris,

Forms for Abhik Das are now complete.

Thanks very much,

Brendan

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Wednesday, February 24, 2010 5:15 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Abel, Brendan; Archer, Stephanie (NIH/NICHD) [E]; Das, Abhik
Subject: RE: Saturation paper and copyright form

Hi,

Faxed Abhik's yesterday and again just now. Also emailed twice (both times it was kicked back).

Brendan, please let me know you still have not received this.

Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 4:59 PM
To: 'Finer, Neil'; Das, Abhik; Ambal (ambal@uab.edu); 'Brenda Morris'; Laroia, Nirupama
Cc: 'Abel, Brendan'; Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin
Subject: Saturation paper and copyright form
Importance: High

Hi,

NEJM is missing your copyright form for the saturation paper. Please fill in the information and either fax it (781) 207.6529 or email a pdf with your signature to Brendan Abel. The information for the manuscript is as follows:

Manuscript number 09-11781

Author – Wally Carlo

Title Oxygen saturation targets in Extremely Preterm Infants

Thanks for your prompt attention

Rose

Thanks for your prompt attention

Rose

09-11781 Carlo

Oxygen Saturation Targets in Extremely Preterm Infants:

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
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higginsr@mail.nih.gov

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Subject: New England Journal of Medicine - 09-11781.R2
Date: Wednesday, February 24, 2010 5:52:02 PM

Dear Dr. Carlo and co-authors,

Thank you for submitting your revision, of "Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial" to the New England Journal of Medicine.

Your submission will be forwarded to the editor, and may be sent out for review as necessary.

Please call us at 617-734-9800 if you have any questions.

Sincerely,

Jeffrey M. Drazen, M.D.
Editor-in-Chief
New England Journal of Medicine
Distinguished Parker B. Francis Professor of Medicine
Harvard Medical School

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Poindexter, Brenda B"
Subject: RE: SUPPORT copyright for CPAP Paper
Date: Wednesday, February 24, 2010 4:59:00 PM

I think you submitted the ICMJE form – this is the copyright form – if already done,
thanks
Rose

From: Poindexter, Brenda B [mailto:bpoindex@iupui.edu]
Sent: Wednesday, February 24, 2010 4:55 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT copyright for CPAP Paper

Sent earlier this afternoon

Sent from my iPhone

On Feb 24, 2010, at 4:53 PM, "Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov> wrote:

Hi,
NEJM is missing your copyright form for the CPAP surf paper. Please fill in the
information and either fax it (781) 207.6529 or email a pdf with your signature to
Brendan Abel. The information for the manuscript is as follows:

Manuscript number 09-11783
Author - Neil Finer
Title Early CPAP versus Surfactant in Extremely Preterm Infants

Thanks for your prompt attention

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

<NEJM-CTA-2009 (2).pdf>

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ed Donovan"; "Brenda Morris"; "Laroia, Nirupama"; "Poindexter, Brenda B"
Cc: "Abel, Brendan"; Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT copyright for CPAP Paper
Date: Wednesday, February 24, 2010 4:52:00 PM
Attachments: NEJM-CTA-2009 (2).pdf

Hi,
NEJM is missing your copyright form for the CPAP surf paper. Please fill in the information and either fax it (781) 207.6529 or email a pdf with your signature to Brendan Abel. The information for the manuscript is as follows:

Manuscript number 09-11783
Author - Neil Finer
Title Early CPAP versus Surfactant in Extremely Preterm Infants

Thanks for your prompt attention

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
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Bethesda, MD 20892
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Contribution Number: _____

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Corresponding Author: _____

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If author was a U.S. Government employee at the time the article was written, please check below.

AGREED TO THIS DAY OF _____ / _____ / _____

(_____)

PRINTED NAME _____

SIGNATURE _____

From: Sood, Beena
To: "Abel, Brendan"
Cc: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 4:43:19 PM
Attachments: [ICMJE-Disclosure-Form-102309_NCPAP.pdf](#)
[ICMJE-Disclosure-Form-102309_SpO2.pdf](#)

Please find attached the ICMJE's for the SUPPORT papers – Please let me know if this is not the correct format

Thanks
Beena

Beena G. Sood, MD, MS
Assistant Professor, Department of Pediatrics
Wayne State University
Associate Neonatologist
Children's Hospital of Michigan
Hutzel Women's Hospital
Tel (Direct): 313-745-5091
Tel (Lab): 313-577-9936
Tel (Adm Office): 313-745-5638
Fax: 313-745-5867
Pager: 313-745-0203, #2579
Cell: 313-590-6837

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 12:05 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; 'Michael O` Shea'; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; Sood, Beena
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
Subject: ICMJE's for SUPPORT papers
Importance: High

Hi,
Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institutes of Health
6100 Executive Blvd., Room 4B03
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INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Beena

Surname:
(or last)

Sood

Effective Date:

21-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Neil N. Finer, MD

Manuscript Title:

Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funding for study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form



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Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

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If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Beena

Surname:
(or last)

Sood

Effective Date:

21-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Waldemar A. Carlo

Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funding for study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +

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Save Form

From: Abel, Brendan
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 4:35:39 PM
Attachments: Support trials form updates.doc

Rose,

We're making progress. Here is updated list. I'll keep letting them come in until tomorrow afternoon; then we can send a final (stern) email to any authors w/ outstanding forms. I think if we have all in by Friday AM we should be good.

Thanks (yet again),

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 12:05 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; 'Michael O`Shea'; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; Abel, Brendan
Subject: ICMJE's for SUPPORT papers
Importance: High

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

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persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

09-11783 Neil Finer

Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Missing Copyright Transfer Form

~~Yoder~~

Donovan

Morris

Laroia

Poindexter

Missing ICMJE Disclosure Form

~~Carlo~~

Walsh (Rec'd form, but consulting fee row in Sec. 2 not completed.)

~~Laptook~~

~~Yoder~~

Faix

Poole

Ambalavanan

Donovan

Newman

Sanchez

~~Poindexter~~

~~Cotton~~

Van Muers

Sood

~~Duara~~

O'Shea

~~Bell~~

Bhandari

Watterberg

09-11781 Carlo

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Missing Copyright Transfer Form

Finer

Das

Ambalavanan

Morris

Laroia

Missing ICMJE Disclosure Form

~~Carlo~~

~~Laptook~~

~~Yoder~~

~~Faix~~

~~Poole~~

~~Newman~~

~~Ambalavanan~~

~~Sanchez~~

~~Piazza~~

~~Phelps~~

~~Poindexter~~

~~Cotton~~

~~Van Meurs~~

~~Duara~~

~~Sood~~

~~O'Shea~~

~~Bell~~

~~Ehrenkranz~~

~~Watterberg~~

Blansfield, Earl (NIH/NICHD) [E]

From: Heather Shinn <HShinn@salud.unm.edu>
Sent: Wednesday, February 24, 2010 1:49 PM
To: Brendan 'Abel' <babel@nejm.org>
Cc: Kristi Watterberg
Subject: Fwd: ICMJE's for SUPPORT papers
Attachments: ICMJE CPAP paper.pdf; ICMJE sat paper.pdf

Brendan,
The forms for ICMJE CPAP and ICMJE Sat Paper for Kristi Watterberg are attached.
Please let me know if you have any questions.
Thank you.
-Heather

Admin Asst III to:
-Dr. Kristi Watterberg
-Dr. Andrea Duncan
-Dr. Erika Fernandez
Dept of Pediatrics/Neonatology
ACC-3 West
2211 Lomas Blvd NE
Albuquerque, NM 87131
(505) 272-0180

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov>
>>> 2/24/2010 10:04 AM >>>

Hi,
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Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network Pregnancy and Perinatology Branch Center for Developmental Biology and Perinatal Medicine Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +

**Use this section to provide any needed explanation

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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5. Nonfinancial associations.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD		Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Abel, Brendan
To: "Phelps, Dale"
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT forms
Date: Wednesday, February 24, 2010 1:42:32 PM

Perfect.

Thanks,

Brendan

From: Phelps, Dale [mailto:Dale_Phelps@URMC.Rochester.edu]
Sent: Wednesday, February 24, 2010 12:44 PM
To: Abel, Brendan
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT forms

As requested, updated since Jan. 2010.
Dale Phelps

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 9:12 AM
To: richard.ehrenkranz@yale.edu; Vivek Narendran; Phelps, Dale; Anthony Piazza
(Anthony.Piazza@oz.ped.emory.edu)
Cc: 'Abel, Brendan'
Subject: SUPPORT forms

Hi all,

Please fill out the attached form, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Abel, Brendan
To: "Michael Cotten"; Archer, Stephanie (NIH/NICHD) [E]
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 1:27:56 PM
Attachments: [Cotten ICMJE disclosure form 09-11781.pdf](#)
[Cotten ICMJE Disclosure form 09-11783.pdf](#)

Dear Dr. Cotten,

For the form for 09-11781, please confirm that the form still looks correct. I just went in and clicked "No" on a couple of boxes in Section 2 to complete it.

For the form for 09-11783, please complete Section 2. Please be sure there are two check marks on each row. You can then email the completed version to me.

Thanks,

Brendan

From: Michael Cotten [mailto:cotte010@mc.duke.edu]
Sent: Wednesday, February 24, 2010 12:26 PM
To: Archer, Stephanie (NIH/NICHD) [E]; Abel, Brendan
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: ICMJE's for SUPPORT papers

Hi Brendan...

I am enclosing my forms below for the two manuscripts. Thank you very much.

mc

C. Michael Cotten MD MHS
Associate Professor of Pediatrics
Medical Director Neonatology Clinical Research
Duke University Medical Center
Box 2739 DUMC
Durham, NC 27710
2424 Erwin Road Suite 504
Durham, NC 27705
ph: 919-681-6024
fax: 919-681-6065
email: cotte010@mc.duke.edu

"Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov>

02/24/2010 12:07 PM

To "Duara, Shahnaz" <SDuara@med.miami.edu>,
"Roger.Faix@hsc.utah.edu" <Roger.Faix@hsc.utah.edu>,
"kwatterberg@salud.unm.edu" <kwatterberg@salud.unm.edu>, "Bell,
Edward" <edward-bell@uiowa.edu>, "Wally Carlo, M.D."
<WCarlo@peds.uab.edu>, "cotte010@mc.duke.edu"
<cotte010@mc.duke.edu>, "alaptook@VMHRI.org"

<alaptook@WHRI.org>, nancy newman <nxs5@case.edu>, "Michael O'Shea" <moshea@wfubmc.edu>, "Poindexter, Brenda B" <bpoindex@iupui.edu>, "Pablo.Sanchez@UTSouthwestern.edu" <Pablo.Sanchez@UTSouthwestern.edu>, "bsood@med.wayne.edu" <bsood@med.wayne.edu>

cc "Archer, Stephanie (NIH/NICHD) [E]" <archerst@mail.nih.gov>, "Abel, Brendan" <babel@nejm.org>

Subject ICMJE's for SUPPORT papers

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institutes of Health

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

[attachment "ICMJE CPAP paper.pdf" deleted by Michael Cotten/Pediatrics/mc/Duke]

[attachment "ICMJE sat paper.pdf" deleted by Michael Cotten/Pediatrics/mc/Duke]

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INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Charles

Surname:
(or last)

Cotten

Effective Date:

24-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	As a member site of the NICHD Neonatal Research Network Duke receives a base award which includes support for a study coordinator and the Principle investigator and alternate PI. There is also indirect support that goes to the institution. The NICHD also provided additional financial support per patient enrolled to help cover costs of research staff enrolling patients and conducting the study.	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
 Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

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Section 1. Identifying Information.

Given Name:
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Surname:
(or last)

Cotten

Effective Date:

24- February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Early CPAP versus Surfactant in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11783

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	As a member site of the NICHD Neonatal Research Network Duke receives a base award which includes support for a study coordinator and the Principle investigator and alternate PI. Ther is also indirect support that goest to the instistution. The NICHD also provided additional financial support per patient enrolled to help cover costs of research staff enrolling patients and conducting the study.	Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.



From: Abel, Brendan
To: "Michael O' Shea"
Cc: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 1:19:06 PM

Great. You're all set.

Thanks,

Brendan

From: Michael O' Shea [mailto:moshea@wfubmc.edu]
Sent: Wednesday, February 24, 2010 12:20 PM
To: Abel, Brendan
Cc: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers

Dear Brendan,
The attached forms are for Michael O'Shea

Thank you,

Michael O'Shea, MD, MPH
Professor of Pediatrics
Wake Forest University School of Medicine

phone (336)-716-4663
FAX (336)-716-2525
email moshea@wfubmc.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 12:05 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; Michael O' Shea; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
Subject: ICMJE's for SUPPORT papers
Importance: High

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Bell, Edward"
Subject: RE: CONFIDENTIAL SUPPORT CPAP paper resubmission
Date: Wednesday, February 24, 2010 1:16:00 PM

They have not been changed

Rose

From: Bell, Edward [mailto:edward-bell@uiowa.edu]
Sent: Wednesday, February 24, 2010 1:11 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: CONFIDENTIAL SUPPORT CPAP paper resubmission

What about the tables?

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 11:18 AM
To: 'vineet.bhandari@yale.edu'; (susie.buchter@oz.ped.emory.edu); 'Duara, Shahnaz'; 'Finer, Neil'; Gantz, Marie; Laroia, Nirupama; 'Brenda Morris'; nancy newman; 'Michael O`Shea'; 'Poole Kenneth (E-mail)'; Rich, Wade; bsood@med.wayne.edu; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Bell, Edward; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; MICKey Caplan; Oh William (E-mail); Pablo Sanchez; Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Zaterka-Baxter, Kristin'; 'Huitema, Carolyn Petrie'; 'Cunningham, Meg'
Subject: CONFIDENTIAL SUPPORT CPAP paper resubmission

Hi,

NEJM asked for some minor clarifications on the CPAP paper. Attached is the most recent version which has gone back to the editors. I will keep everyone posted of any progress.

If you received an email regarding your ICJME form, please complete and return to Brendan Abel ASAP. IF you did not get a separate email, you do not need to do anything.

Thanks for all your help!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852

301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Bell, Edward](#)
To: [Abel, Brendan](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: FW: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 1:03:47 PM
Attachments: [NEJM CPAP disclosure - Bell.pdf](#)
[NEJM ROP disclosure - Bell.pdf](#)
Importance: High

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, February 24, 2010 11:05 AM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; 'Michael O` Shea'; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
Subject: ICMJE's for SUPPORT papers
Importance: High

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higginsr@mail.nih.gov



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

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2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Edward

Surname:
(or last)

Bell

Effective Date:

07-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Neil N. Finer

Manuscript Title:

Early CPAP versus surfactant in very preterm infants: the SUPPORT trial

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	University of Iowa	The University reimburses, with funds from my NIH grant, my travel costs to attend the meetings of the NICHD Neonatal Research Network	Del ×
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Save Form



ICMJE

INTERNATIONAL COMMITTEE *of*
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	University of Iowa	The University reimburses, with funds from my NIH grant, my travel costs to attend the meetings of the NICHD Neonatal Research Network	Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Save Form

From: Phelps, Dale
To: Abel, Brendan
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT forms
Date: Wednesday, February 24, 2010 12:46:06 PM
Attachments: ICMJE_sat_paperUniform Disclosure.pdf

As requested, updated since Jan. 2010.
Dale Phelps

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 9:12 AM
To: richard.ehrenkranz@yale.edu; Vivek Narendran; Phelps, Dale; Anthony Piazza
(Anthony.Piazza@oz.ped.emory.edu)
Cc: 'Abel, Brendan'
Subject: SUPPORT forms

Hi all,
Please fill out the attached form, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help!
Rose

Rosemary D. Higgins, MD
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National Institutes of Health
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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Dale

Surname:
(or last)

Phelps

Effective Date:

24-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH / NICHD	5% PI support, Coordinator effort, supplies	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH/NICHD	Travel for planning and monitoring meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD/NIH	Funds to purchase equipment for the study	Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD		Del X
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD		Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: [Bradley Yoder](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT FORMS
Date: Wednesday, February 24, 2010 12:34:02 PM

Done.

Brad Yoder
Division of Neonatology
University of Utah SOM

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 10:09 AM
To: Bradley Yoder
Cc: 'Abel, Brendan'
Subject: SUPPORT FORMS

Brad

Your forms were incomplete for NEJM. You need to choose either yes or no under the "To Your Institution" in the consulting row. Please return the forms directly to Brendan at NEJM.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

Higgins, Rosemary (NIH/NICHD) [E]

From: Michael O'Shea <moshea@wfubmc.edu>
Sent: Wednesday, February 24, 2010 12:20 PM
To: Abel, Brendan
Cc: Archer, Stephanie (NIH/NICHD) [E]; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: ICMJE's for SUPPORT papers
Attachments: ICMJE CPAP paper - OShea.pdf; ICMJE sat paper-OShea.pdf

Dear Brendan,
The attached forms are for Michael O'Shea

Thank you,

Michael O'Shea, MD, MPH
Professor of Pediatrics
Wake Forest University School of Medicine

phone (336)-716-4663
FAX (336)-716-2525
email moshea@wfubmc.edu

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 24, 2010 12:05 PM
To: 'Duara, Shahnaz'; Roger.Faix@hsc.utah.edu; kwatterberg@salud.unm.edu; Bell, Edward; Wally Carlo, M.D.; cotte010@mc.duke.edu; alaptook@WIHRI.org; nancy newman; Michael O'Shea; 'Poindexter, Brenda B'; Pablo.Sanchez@UTSouthwestern.edu; bsood@med.wayne.edu
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Abel, Brendan'
Subject: ICMJE's for SUPPORT papers
Importance: High

Hi,
Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Subject: update
Date: Wednesday, February 24, 2010 12:18:24 PM
Attachments: [Support trials form updates.doc](#)

Hi Rose,

I think we're now on our way to getting this taken care of. I've attached an updated form that lists all missing forms. Let me know if there is anything I can do. I'll send you another update as we get closer.

Thanks very much,

Brendan

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

09-11783 Neil Finer

Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Missing Copyright Transfer Form

Yoder
Donovan
Morris
Laroia
Poindexter

Missing ICMJE Disclosure Form

Carlo
Walsh (Rec'd form, but consulting fee row in Sec. 2 not completed.)
Laptook
Yoder
Faix
Poole
Ambalavanan
Donovan
Newman
Sanchez
Poindexter
Cotton
Van Muers
Sood
Duara
O'Shea
Bell
Bhandari
Watterberg

09-11781 Carlo

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Missing Copyright Transfer Form

Finer
Das
Ambalavanan
Morris
Laroia

Missing ICMJE Disclosure Form

Carlo

Laptook

Yoder

Faix

Poole

Newman

Ambalavanan

Sanchez

Piazza

Phelps

Poindexter

Cotton

Van Meurs

Duara

Sood

O'Shea

Bell

Ehrenkranz

Watterberg

From: [Gantz, Marie](#)
To: [Abel, Brendan](#); [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT FORMS
Date: Wednesday, February 24, 2010 12:16:43 PM

Thanks, Brendan. Let me know if there is anything else I need to do.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-8255

From: [Abel, Brendan \[mailto:babel@nejm.org\]](mailto:babel@nejm.org)
Sent: Wednesday, February 24, 2010 12:16 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'; Gantz, Marie
Subject: RE: SUPPORT FORMS

Hi Marie,

I actually have the properly filled out forms on file for you. So you're all set!

Thanks,

Brendan

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\] \[mailto:higginsr@mail.nih.gov\]](mailto:higginsr@mail.nih.gov)
Sent: Wednesday, February 24, 2010 12:08 PM
To: Gantz, Marie
Cc: Abel, Brendan
Subject: SUPPORT FORMS

Marie

Brendan Abel needs you to redo your forms to complete section 2 (there should be two checked boxes in each row).

Please return these directly to him at NEJM.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "richard.ehrenkranz@yale.edu"; "Vivek Narendran"; "Phelps, Dale"; "Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu)"
Cc: "Abel, Brendan"
Subject: SUPPORT forms
Date: Wednesday, February 24, 2010 12:11:00 PM
Attachments: ICMJE sat paper.pdf

Hi all,

Please fill out the attached form, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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For overnight delivery use Rockville, MD 20852
301-496-5575
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higginsr@mail.nih.gov



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
- Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

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At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Bradley Yoder"
Cc: "Abel, Brendan"
Subject: SUPPORT FORMS
Date: Wednesday, February 24, 2010 12:09:00 PM
Attachments: ICMJE CPAP paper.pdf
ICMJE sat paper.pdf

Brad

Your forms were incomplete for NEJM. You need to choose either yes or no under the "To Your Institution" in the consulting row. Please return the forms directly to Brendan at NEJM.

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

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Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Early CPAP versus Surfactant in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
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						Add +
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						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Gantz, Marie"
Cc: "Abel, Brendan"
Subject: SUPPORT FORMS
Date: Wednesday, February 24, 2010 12:07:00 PM
Attachments: ICMJE CPAP paper.pdf
ICMJE sat paper.pdf

Marie

Brendan Abel needs you to redo your forms to complete section 2 (there should be two checked boxes in each row).

Please return these directly to him at NEJM.

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov



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No

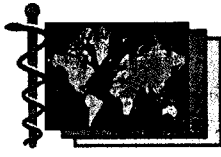
Yes, specify nature of compensation

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						Add +
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						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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						Add +
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						Add +
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Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Duara, Shahnaz"; "Roger.Faix@hsc.utah.edu"; "kwatterberg@salud.unm.edu"; "Bell, Edward"; "Wally Carlo, M.D."; "cotte010@mc.duke.edu"; "alaptook@WIHRI.org"; "nancy.newman"; "Michael O'Shea"; "Poindexter, Brenda B"; "Pablo.Sanchez@UTSouthwestern.edu"; "bsood@med.wayne.edu"
Cc: Archer, Stephanie (NIH/NICHD) [E]; "Abel, Brendan"
Subject: ICMJE's for SUPPORT papers
Date: Wednesday, February 24, 2010 12:04:00 PM
Attachments: [ICMJE CPAP paper.pdf](#)
[ICMJE sat paper.pdf](#)
Importance: High

Hi,

Please fill out the attached two forms, save the form, and email it to Brendan Abel at NEJM. I have copied Brendan on this email, so you have his email address. The form must be filled out and submitted in the interactive form. **Please do this today or tomorrow.**

Thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov



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09-11783

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Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

A Randomized Trial of Oxygen Saturation Targets in Extremely Preterm Infants

Manuscript Identifying Number (if you know it):

09-11781

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						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
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						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del ×
						Add +



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From: Abel, Brendan
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@NIH.NICHHD)
Subject: RE: 09-11783
Date: Wednesday, February 24, 2010 11:38:32 AM

Hi Rose,

All copyrights are fine in this format. But as I explained earlier, we need the disclosure forms to be filled out electronically and emailed in their original interactive format (as attached). So unfortunately none of them that were just emailed are acceptable. I'm in the process of creating a sheet that lists all missing forms which I'll pass along shortly.

Thanks,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Wednesday, February 24, 2010 11:04 AM
To: Abel, Brendan
Subject: 09-11783

Hi Brendan

Here are two files that contain copyright forms and ICMJE forms for the Finer CPAP paper.

Let me know if these are ok or if you need on-line submissions from any of the authors. We will try to have everything back for this paper and the other paper (Dr. Carlo) shortly.

Thanks for all your help

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

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persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

From: Gantz, Marie
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT Oximeters used for Physio Challenge, 2009-11.xls
Date: Tuesday, February 23, 2010 4:46:58 PM

Thanks.

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 23, 2010 4:46 PM
To: Gantz, Marie
Cc: 'Finer, Neil'; Wally Carlo, M.D.
Subject: FW: SUPPORT Oximeters used for Physio Challenge, 2009-11.xls

Here it is

Rose

From: Archer, Stephanie (NIH/NICHD) [E]
Sent: Tuesday, February 23, 2010 4:10 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT Oximeters used for Physio Challenge, 2009-11.xls

Here are the survey results.

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]; Irene, Amanda
Subject: RE:
Date: Tuesday, February 23, 2010 3:37:31 PM

Thanks.

Amanda – please copy and paste this into the minutes for SUPPORT!

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 23, 2010 3:37 PM
To: Cunningham, Meg; Irene, Amanda
Subject:

FOR THE MINUTES!!

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE:
Date: Tuesday, February 23, 2010 12:33:57 PM

Sounds good.

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Tuesday, February 23, 2010 12:31 PM
To: Abel, Brendan
Subject: RE:

The one with NIH Support

We will work on the rest of them today for both papers.

Thanks

Rose

From: Abel, Brendan [<mailto:babel@nejm.org>]
Sent: Tuesday, February 23, 2010 12:30 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE:

Hi Rose,

I just received two different versions of Larioa's disclosure form. One w/ NIH support, one w/ nothing disclosed. Please let me know which one to use.

Thanks,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Tuesday, February 23, 2010 12:22 PM
To: Abel, Brendan
Subject: FW:

From: Larioia, Nirupama [mailto:Nirupama_Larioia@URMC.Rochester.edu]
Sent: Monday, February 22, 2010 2:31 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject:

Apologies for the delay.

Nirupama Larioia

This email message is a private communication. The information transmitted, including attachments, is intended only for the person or entity to which it is addressed and may contain confidential, privileged, and/or proprietary material. Any review, duplication, retransmission, distribution, or other use of, or taking of any action in reliance upon, this information by persons or entities other than the intended recipient is unauthorized by the sender and is prohibited. If you have received this message in error, please contact the sender immediately by return email and delete the original message from all computer systems. Thank you.

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abel, Brendan"
Subject: FW: NEJM SUPPORT TRIAL
Date: Tuesday, February 23, 2010 12:20:00 PM
Attachments: [ICMJE-Disclosure-Form-102309_CPAP.pdf](#)
[ICMJE-Disclosure-Form-102309_oxygen_saturation.pdf](#)

From: Laroia, Nirupama [mailto:Nirupama_Laroia@URMC.Rochester.edu]
Sent: Monday, February 22, 2010 3:22 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: NEJM SUPPORT TRIAL

Dear Dr. Higgins,

I do not seem to have the correct e-mail address for Stephanie Archer.

I have not faxed the copyright forms, as I need to know the contribution number (or I could leave it blank and it can be filled later). Please let me know so that I can fax the forms to you. Thanks.

Nirupama

From: Laroia, Nirupama
Sent: Monday, February 22, 2010 2:58 PM
To: 'archers@mail.nih.gov'
Cc: 'higginsr@mail.nih.gov'
Subject: NEJM SUPPORT TRIAL

Hi Stephanie,

1. FINANCIAL DISCLOSURE

Attached is the requested copy of my Financial Disclosure for the SUPPORT Saturation paper. I apologize for the delay in getting this to you.

I have not uploaded it to the nejm site, please let me know if you need me to do that.

2. COPYRIGHT FORM

I am going to fax you the copyright forms today. Please let me know if there is anything else you need me to do.

Please ask Dr. Higgins to ignore the form I sent her earlier today. Thanks.

Nirupama Laroia, MD
Assoc. Professor, Dept of Pediatrics/ Neonatology
Golisano Children's Hospital at Strong, University of Rochester
601 Elmwood Ave, Box 651, Rochester, NY 14642
Phone: 585 275 2972, Fax: 585 461 3614



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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

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5. Nonfinancial associations.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:
 (or first) (or last) Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
 Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH-NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	For travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Grant supported working meetings	Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

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						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

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5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH- NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Study related meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

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Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abel, Brendan"
Subject: FW: NEJM SUPPORT TRIAL
Date: Tuesday, February 23, 2010 12:20:00 PM
Attachments: ICMJE-Disclosure-Form-102309_CPAP.pdf
ICMJE-Disclosure-Form-102309_oxygen saturation.pdf

From: Laroia, Nirupama [mailto:Nirupama_Laroia@URMC.Rochester.edu]
Sent: Monday, February 22, 2010 2:58 PM
To: 'archers@mail.nih.gov'
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: NEJM SUPPORT TRIAL

Hi Stephanie,

1. FINANCIAL DISCLOSURE

Attached is the requested copy of my Financial Disclosure for the SUPPORT Saturation paper. I apologize for the delay in getting this to you. I have not uploaded it to the nejm site, please let me know if you need me to do that.

2. COPYRIGHT FORM

I am going to fax you the copyright forms today. Please let me know if there is anything else you need me to do.

Please ask Dr. Higgins to ignore the form I sent her earlier today. Thanks.

Nirupama Laroia, MD
Assoc. Professor, Dept of Pediatrics/ Neonatology
Golisano Children's Hospital at Strong, University of Rochester
601 Elmwood Ave, Box 651, Rochester, NY 14642
Phone: 585 275 2972, Fax: 585 461 3614



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

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2. The work under consideration for publication.

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Nirupama

Surname:
(or last)

Laroia

Effective Date:

19-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Neil Finer

Manuscript Title:

Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH-NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	For travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Grant supported working meetings	Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
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							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
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						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
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						Add +
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						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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Save Form



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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
 Yes, specify nature of compensation

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH- NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Study related meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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							Add +
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Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Save Form

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Webb, Robin E."
Subject: RE: SUPPORT Intermittent Hypoxia
Date: Tuesday, February 23, 2010 12:00:00 PM

Use the same as I just sent

Rose

From: Webb, Robin E. [mailto:rwebb@rti.org]
Sent: Tuesday, February 23, 2010 11:56 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; Wally Carlo, M.D.; mcw3@case.edu; Bradley Yoder; Roger Faix; alaptook@WIHRI.org; kurt.schibler@cchmc.org; Das, Abhik; Wallace, Dennis; nancy newman; Rich, Wade; Gantz, Marie
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; Webb, Robin E.; Irene, Amanda
Subject: SUPPORT Intermittent Hypoxia

Please send your availability for the days below, indicating time zone if other than ET.

Thanks,
Robin

Mon 3/1
Tues 3/2
Wed 3/3
Thurs 3/4
Fri 3/5

Mon 3/8
Tues 3/9
Wed 3/10
Thurs 3/11
Fri 3/12

Mon 3/15
Tues 3/16
Wed 3/17
Thurs 3/18
Fri 3/19

Mon 3/22
Tues 3/23
Wed 3/24
Thurs 3/25
Fri 3/26

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, February 22, 2010 11:16 AM
To: Finer, Neil; 'Wally Carlo, M.D.'; mcw3@case.edu; 'Bradley Yoder'; Roger Faix; alaptook@WIHRI.org; Kurt Schibler [kurt.schibler@cchmc.org]; Das, Abhik; Wallace, Dennis; nancy newman; Rich, Wade; Gantz, Marie
Cc: Archer, Stephanie (NIH/NICHD) [E]; Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn

Petrie; Webb, Robin E.
Subject: SUPPORT Intermittent Hypoxia

Hi,
Attached is a secondary study fro review.
I will have Robin set up a call to discuss.

Thanks
Rose

From: [Krisa Van Meurs](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: SUPPORT PAPERS
Date: Monday, February 22, 2010 6:15:33 PM

Hi Rose,
Yes, I sent in 2 scanned forms when the first request went out. I will contact NEJM to see if they received them.
Best,
Krisa

>Krisa
>Did you submit your ICMJE form on-line for the SUPORT papers?
>
>Thanks
>Rose
>
>Rosemary D. Higgins, MD
>Program Scientist for the Neonatal Research Network
>Pregnancy and Perinatology Branch
>Center for Developmental Biology and Perinatal Medicine
>Eunice Kennedy Shriver National Institute of Child Health and Human
>Development
>National Institutes of Health
>6100 Executive Blvd., Room 4B03
>MSC 7510
>Bethesda, MD 20892
>For overnight delivery use Rockville, MD 20852
>301-496-5575
>301-496-3790 (FAX)
>higginsr@mail.nih.gov
>

From: Roger Faix
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT FU
Date: Monday, February 22, 2010 5:17:10 PM

Thanks, Rose! Feedback is always welcome.

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Monday, February 22, 2010 8:34 AM
To: Roger Faix; Bradley Yoder; 'Anna Bodnar'; Karen Osborne RN; Shawna Baker
Cc: Gantz, Marie
Subject: SUPPORT FU

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Laroia, Nirupama
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: NEJM SUPPORT TRIAL
Date: Monday, February 22, 2010 3:21:41 PM
Attachments: [ICMJE-Disclosure-Form-102309_CPAP.pdf](#)
[ICMJE-Disclosure-Form-102309_oxygen saturation.pdf](#)

Dear Dr. Higgins,

I do not seem to have the correct e-mail address for Stephanie Archer.

I have not faxed the copyright forms, as I need to know the contribution number (or I could leave it blank and it can be filled later). Please let me know so that I can fax the forms to you. Thanks.

Nirupama

From: Laroia, Nirupama
Sent: Monday, February 22, 2010 2:58 PM
To: 'archers@mail.nih.gov'
Cc: 'higginsr@mail.nih.gov'
Subject: NEJM SUPPORT TRIAL

Hi Stephanie,

1. FINANCIAL DISCLOSURE

Attached is the requested copy of my Financial Disclosure for the SUPPORT Saturation paper. I apologize for the delay in getting this to you.

I have not uploaded it to the nejm site, please let me know if you need me to do that.

2. COPYRIGHT FORM

I am going to fax you the copyright forms today. Please let me know if there is anything else you need me to do.

Please ask Dr. Higgins to ignore the form I sent her earlier today. Thanks.

Nirupama Laroia, MD
Assoc. Professor, Dept of Pediatrics/ Neonatology
Golisano Children's Hospital at Strong, University of Rochester
601 Elmwood Ave, Box 651, Rochester, NY 14642
Phone: 585 275 2972, Fax: 585 461 3614



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Nirupama

Surname:
(or last)

Laroia

Effective Date:

19-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Neil Finer

Manuscript Title:

Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11783

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH-NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	For travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Grant supported working meetings	Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form



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Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

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4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH- NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH-NICHD	Study related meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

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- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

From: Michael Cotten
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT FU
Date: Monday, February 22, 2010 2:40:43 PM

thanks Rose.

mc
C. Michael Cotten MD MHS
Associate Professor of Pediatrics
Medical Director Neonatology Clinical Research
Duke University Medical Center
Box 2739 DUMC
Durham, NC 27710
2424 Erwin Road Suite 504
Durham, NC 27705
ph: 919-681-6024
fax: 919-681-6065
email: cotte010@mc.duke.edu

"Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov>

02/22/2010 10:33 AM

To Ronald N Goldberg <goldb008@mc.duke.edu>, "Ricki F Goldstein"
<golds005@mc.duke.edu>, Michael Cotten
<cotte010@mc.duke.edu>, "Kimberley A Fisher"
<kimberley.fisher@duke.edu>, "sandra.grimes@duke.edu"
<sandra.grimes@duke.edu>

cc "Gantz, Marie" <mgantz@rti.org>

Subject SUPPORT FU

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
 Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852

301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Zaterka-Baxter, Kristin
To: Abel, Brendan; Das, Abhik
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Request for forms for saturation SUPPORT paper
Date: Monday, February 22, 2010 1:25:40 PM
Attachments: [09-11783_ICMJE-Disclosure-Form-102309_Das \(2\).pdf](#)
[09-11781_ICMJE-Disclosure-Form-102309_Das \(2\).pdf](#)
[11783_Copyright_Das.pdf](#)
[11781_Copyright_Das.pdf](#)

On behalf of Dr. Das, please see attached.

Thanks and please let me know if you need anything further.
Kris

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Monday, February 22, 2010 1:02 PM
To: Zaterka-Baxter, Kristin; Das, Abhik
Cc: 'higginsr@mail.nih.gov'
Subject: RE: Request for forms for saturation SUPPORT paper

Dear Dr. Das,

Thank you for sending in your forms. Journal policy dictates that we receive a signed copyright transfer form for each manuscript (09-11783- Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial and 09-11781 Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial).

The same applies to the disclosure form- please provide me with a form for each manuscript. Please also be sure to indicate the name of the entity from which you received grant support on each form.

You can email all forms back to me.

Thanks,

Brendan Abel
Editorial Assistant
New England Journal of Medicine

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, February 22, 2010 12:51 PM
To: Abel, Brendan
Subject: FW: Request for forms for saturation SUPPORT paper
Importance: High

Here is Dr. Das's form. I will also get the co-authors to send you the forms directly

Thanks for all your help

Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]

Sent: Monday, February 22, 2010 10:31 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: Request for forms for saturation SUPPORT paper
Importance: High

Hi,

Abhik thought he completed these but asked that I send just in case.
Thanks,
Kris

-----Original Message-----

From: Das, Abhik
Sent: Saturday, February 20, 2010 10:39 PM
To: Zaterka-Baxter, Kristin
Subject: FW: Request for forms for saturation SUPPORT paper
Importance: High

I think I did this but am not sure. Can you do this for me anyway?

Abhik Das
Senior Research Statistician
RTI International

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 08:52 AM Eastern Standard Time
To: Das, Abhik; bsood@med.wayne.edu; 'Brenda Poindexter'; Brenda Morris;
Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Gantz, Marie; Laroia,
Nirupama; 'Michael O'Shea'; Poole, W. Kenneth; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: Request for forms for saturation SUPPORT paper

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Let me know if there are any questions.

The title of the paper is:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

The manuscript number is 09-11781

Waldemar A. Carlo is the corresponding author

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human
Development

National Institutes of Health

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

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Surname:
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							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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						Add +
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						Add +
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						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
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						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Short Title or description of Contribution: Oxygen Saturation Targets in Extremely Preterm
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SIGNATURE Abhik Das

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abel, Brendan"
Subject: FW: Request for forms for saturation SUPPORT paper
Date: Monday, February 22, 2010 12:51:00 PM
Attachments: ICMJE-Disclosure-Form-102309 Das.pdf
Das.jpg
Importance: High

Here is Dr. Das's form. I will also get the co-authors to send you the forms directly

Thanks for all your help

Rose

From: Zaterka-Baxter, Kristin [mailto:kzaterka@rti.org]
Sent: Monday, February 22, 2010 10:31 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: Request for forms for saturation SUPPORT paper
Importance: High

Hi,

Abhik thought he completed these but asked that I send just in case.
Thanks,
Kris

-----Original Message-----

From: Das, Abhik
Sent: Saturday, February 20, 2010 10:39 PM
To: Zaterka-Baxter, Kristin
Subject: FW: Request for forms for saturation SUPPORT paper
Importance: High

I think I did this but am not sure. Can you do this for me anyway?

Abhik Das
Senior Research Statistician
RTI International

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 08:52 AM Eastern Standard Time
To: Das, Abhik; bsood@med.wayne.edu; 'Brenda Poindexter'; Brenda Morris; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Gantz, Marie; Laroia, Nirupama; 'Michael O'Shea'; Poole, W. Kenneth; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
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Let me know if there are any questions.

The title of the paper is:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

The manuscript number is 09-11781

Waldemar A. Carlo is the corresponding author

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Effective Date:

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Are you the corresponding author? Yes No

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

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	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

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- Yes, the following relationships/conditions/circumstances are present (explain below):



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AGREED TO THIS DAY OF 02, 19, 2010 (_____)

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SIGNATURE [Handwritten Signature]

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Karen Osborne RN"
Subject: RE: SUPPORT FU
Date: Monday, February 22, 2010 11:42:00 AM

You are welcome!!

From: Karen Osborne RN [mailto:Karen.Osborne@hsc.utah.edu]
Sent: Monday, February 22, 2010 11:44 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT FU

Thank you!

Karen

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, February 22, 2010 8:34 AM
To: Roger Faix; Bradley Yoder; 'Anna Bodnar'; Karen Osborne RN; Shawna Baker
Cc: Gantz, Marie
Subject: SUPPORT FU

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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For overnight delivery use Rockville, MD 20852
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Abel, Brendan](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: 09-11781
Date: Monday, February 22, 2010 10:43:45 AM
Attachments: [ICMJE Disclosure form.pdf](#)
[NEJM forms Carlo SUPPORT 09-11781 2 of 2.pdf](#)
[NEJM forms Carlo SUPPORT 09-11781 1 of 2.pdf](#)

Not sure what forms you mean.. I've attached a clean version of the form, as well as the forms that you sent me. Let me know if you need anything else.

Thanks,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Monday, February 22, 2010 10:39 AM
To: Abel, Brendan
Cc: 'Wally Carlo, M.D.'
Subject: RE: 09-11781

Can you send me the forms and I will have folks return them directly to you

Thanks
Rose

From: Abel, Brendan [<mailto:babel@nejm.org>]
Sent: Friday, February 19, 2010 3:26 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: 'Wally Carlo, M.D.'
Subject: RE: 09-11781

Hi Rose,

Thanks for sending. Unfortunately, many of the disclosure forms are not filled out correctly. The majority will be a quick fix, but several others need to be filled out electronically.

Most of the forms are correctly filled out, but must be sent in the original pdf format. They should appear just like the attached form, where the form is still in its interactive format. This likely means you'll have to attach each form separately. Feel free to take as many emails as you need. My inbox is used to it. (This applies to Drs. Bell, Carlo, Cotten, Ehrenkrantz, Laptook, Narendran, Newman, O'Shea, Phelps, Piazza, Poindexter, Sanchez, and Sood.)

Drs. Duara, Faix, and Watterberg will need to fill out their forms electronically (rather than handwritten) and send in their original pdf format.

Dr. Gantz needs to complete Sec. 2- there should be two boxes checked in each row. He can see the attached sample for guidance.

Dr. Yoder just needs to choose Yes or No under the "To Your Institution" in consulting row.

The good news is that all copyright transfer forms appear complete.

Let me know if you have any questions. I'll be at my desk for the next hour or so. You're welcome to send at beginning of next week if you don't want to spend your Friday afternoon taking care of this.

Have a nice weekend,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 2:51 PM
To: Abel, Brendan
Cc: 'Wally Carlo, M.D.'
Subject: 09-11781

Hi Brendan,

In an effort to get the required copyright and ICMJE forms for the co-authors for manuscript 09-11781, I am attaching two pdf's which have many of the required forms. Dr. Ivan Franz will submit his forms directly to your office on Monday.

Would it be possible for you to let Wally or I know who is missing (if any)? We can assist the co-authors with completion of the forms.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Section 1. Identifying Information.

Given Name:
(or first)

Surname:
(or last)

Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

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Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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Contribution Number: 09-11781

Short Title or description of Contribution: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets

Corresponding Author: Wally Carlo in Ethnicity Practice Lab

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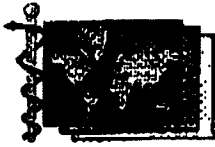
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Corresponding author's name: Wally Carlo

Manuscript Title: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets In Extremely Premature Infants

Manuscript Identifying Number (if you know it): 09-11781

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						Add +
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						Add +
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Short Title or description of Contribution: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

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Corresponding author's name: Waldemar A. Carlo

Manuscript Title: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it): 09-11781

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						Add +
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						Add +
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						Add +
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						Add +
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Corresponding author's name:

Waldemar Carlo, MD

Manuscript Title:

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Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	U10 HD40689	Del x
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Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Cincinnati Site Principal Investigator to attend Steering Committee Meeting
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Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Study Oximeters Provided by Neonatal Network
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

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Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		



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Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
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Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		

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Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funding for study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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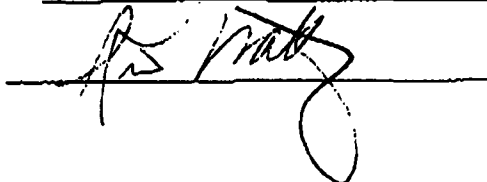
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Grant	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<u>NEONATAL RESEARCH NETWORK</u>	Del x
									Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
									Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
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Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
									Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
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								Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x



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	<i>NO</i>								Add +
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									Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>						Del x
									Add +
Royalties	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
Stock/stock options	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
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									Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
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Corresponding author's name: Neil Finer

Manuscript Title: Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial

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							Add +
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							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH, NICHD	Same	Del x
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							Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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Short Title or description of Contribution: Early CPAP versus surfactant in very preterm infants

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						Add +
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Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
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						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	University of Iowa	The University reimburses, with funds from my NIH grant, my travel costs to attend the meetings of the NICHD Neonatal Research Network	Del X
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Short Title or description of Contribution: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets In Extremely Premature Infants

Corresponding Author: Waldemar Carlo

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Corresponding Author: Waldemar A Carlo in extremely premature infants

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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Duke University	this was a multicenter trial sponsored by NICHD. The institution received capitation payment for study expenses, and a base award was provided to centers in the Network for study personnel and infrastructure.	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		As part of the base award, there is a portion of the overall budget set aside for travel to Network/ study steering committee meetings in the Washington D. C. area at the NIH rate.	Del x
							Add +

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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Type of Relationship (In alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x

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						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Loyalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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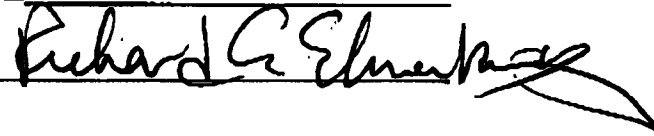
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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD	Salary support for research staff	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Manuscript Title:

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Manuscript Identifying Number (if you know it):

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No

Yes, specify nature of compensation *NICHD Grant #U1A MD 053124*

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
 Yes, the following relationships/conditions/circumstances are present (explain below):

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(or last)

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Effective Date:

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Are you the corresponding author? Yes No

Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it):

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Corresponding author's name:

Waldemar A. Carlo

Manuscript Title:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

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09-11781

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	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eunice Kennedy Shriver National Institute of Child Health and Human Development		Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Contribution Number: 09-11761

Short Title or description of Contribution: Oxygen Saturation Targets: SUPRODTrial

Author: Waldemar Carlo

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 (or first) (or last) Format example: 07-August-2008

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Manuscript Title:

Manuscript Identifying Number (if you know it):

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del X
							Add +
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del X



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment support at NICHD		Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			Del x
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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Employee and Program Scientist	Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
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Short Title or description of Contribution: Randomized Trial of Oxygen Saturation

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Surname:
(or last)

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Corresponding author's name:

Wally Carlo MD

Manuscript Title:

The Support Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it):

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No

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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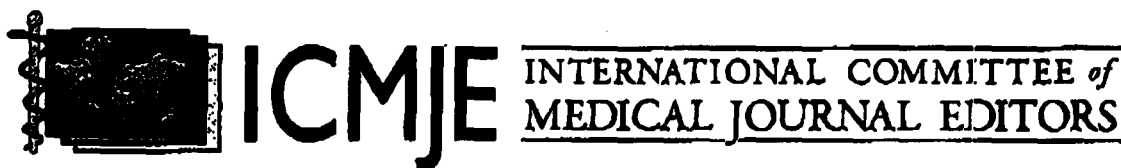
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Narendran

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Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it): 09-11783

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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Short Title or description of Contribution: Oxygen Saturation Targets
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Manuscript Title: Randomize: Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it): 09-11781

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Are you the corresponding author? Yes No

Corresponding author's name: Waldemar Carlo

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							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



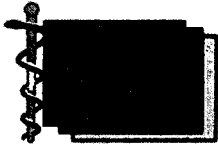
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

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Contribution Number: 09-11781

Short Title or description of Contribution: The SUPPORT TRIAL RCT of O₂ saturations

Corresponding Author: Waldemar A. Carlo

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If author was a U.S. Government employee at the time the article was written, please check below.

AGREED TO THIS DAY OF JAN 27, 2010

PRINTED NAME Dale L Phelps, MD

SIGNATURE Dale L Phelps, MD



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Section 1. Identifying Information.

Given Name:
(or first)

Dale

Surname:
(or last)

Phelps

Effective Date:

27-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

The SUPPORT Trial: Randomized trial of oxygen saturation targets in extremely premature infants

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH - NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	for travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	grant supported working meetings	Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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To: "Kristi Watterberg"; "Cbackstrom@salud.unm.edu"; "Rebecca Montman"; "JaFuller@salud.unm.edu"; "Robin Ohls"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:35:00 AM

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Roger Faix"; "Bradley Yoder"; "Anna Bodnar"; "Karen.Osborne@hsc.utah.edu"; "Shawna Baker"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:34:00 AM

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "ifrantz@tuftsmedicalcenter.org"; "emcgowan@tuftsmedicalcenter.org"; "Furey, Anne M";
"BMackinnon@tuftsmedicalcenter.org"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:33:00 AM

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Ronald N. Goldberg"; "Ricki F. Goldstein"; "Michael Cotten"; "Kimberley A Fisher"; "sandra.grimes@duke.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:32:00 AM

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Richard Ehrenkranz"; "Matthew Bizzarro"; "elaine.romano@yale.edu"; "monica.konstantino@yale.edu"; "Joanne Williams"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:31:00 AM

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

Rose

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Krisa Van Meurs"; "Susan Hintz"; "mbball@stanford.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:31:00 AM

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo Sanchez"; "Roy.Heyne@utsouthwestern.edu"; "Diana Vasil"; "Lizette Torres"; "Nancy Miller"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:30:00 AM

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Rose

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mcw3@case.edu"; "drfjcmd@aol.com"; "nancy.newman"; "Bonnie Siner"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Monday, February 22, 2010 10:29:00 AM

Congratulations!!! Your SUPPORT FU data are all up to date. Keep up the excellent work and thanks for all the effort!!!

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higginsr@mail.nih.gov

From: [Frantz, Ivan](#)
To: [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Subject: RE: SUPPORT Update
Date: Monday, February 22, 2010 10:17:55 AM

Where do I find the copyright and ICMJE forms? When I go to the NEJM author site the Support papers are not listed.

Ivan D. Frantz, III, M.D.
Professor of Pediatrics
Tufts University School of Medicine

Tufts Medical Center Box 44
800 Washington St.
Boston, MA 02111

617 636 5322

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 4:59 PM
To: 'Phelps, Dale'; 'Michael O` Shea'; 'Duara, Shahnaz'; 'Finer, Neil'; Rich, Wade; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); bsood@med.wayne.edu; 'Brenda Morris'; Gantz, Marie; Laroia, Nirupama; Vivek Narendran; 'Poole Kenneth (E-mail)'; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); vineet.bhandari@yale.edu; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Frantz, Ivan; Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Zaterka-Baxter, Kristin; Cunningham, Meg; Carolyn Petrie; Newman, Jamie; 'Irene, Amanda'; Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT Update
Importance: High

Hi,

As you know, the SUPPORT papers were resubmitted to NEJM on 2/12. Wally received a request from Dr. Solomon yesterday stating the following:

I am writing again about your manuscript, "Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial." Your revision has been evaluated by the editors and addresses the key concerns raised previously. However, we do need to ask for some additional changes before it is accepted for publication. Revisions are being completed.

Neil received the following request:

Please send a copy of the revision in a Word (.doc) version to me via email at your soonest convenience.

We will keep folks updated as we here more. If you haven't sent your copyright form or ICMJE disclosure, please do so asap.

Thanks

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "adas@rti.org"
Subject: Re: SUPPORT Update
Date: Sunday, February 21, 2010 7:32:21 AM

Clarification, word-smithing and one item that Marie helped with. They are extremely minor!

Thanks
Rose

----- Original Message -----

From: Das, Abhik <adas@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Sat Feb 20 22:54:16 2010
Subject: RE: SUPPORT Update

Rose
What are the revisions requested for Wally's paper?
Thanks
Abhik

Abhik Das
Senior Research Statistician
RTI International

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, February 19, 2010 04:59 PM Eastern Standard Time
To: 'Phelps, Dale'; 'Michael O'Shea'; 'Duara, Shahnaz'; Finer, Neil; Rich, Wade; Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu); bsood@med.wayne.edu; 'Brenda Morris'; Gantz, Marie; Laroia, Nirupama; Vivek Narendran; Poole, W. Kenneth; 'Nancy Newman'; (susie.buchter@oz.ped.emory.edu); 'vineet.bhandari@yale.edu'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Das, Abhik; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Wallace, Dennis; Ed Bell; Ed Donovan; Ehrenkranz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole, W. Kenneth; Roger Faix; Ronald Goldberg; Seetha Shankaran; Stevenson David (E-mail); [SCRN] Stoll, Barbara; Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Zaterka-Baxter, Kristin; Cunningham, Meg; Huitema, Carolyn Petrie; Newman, Jamie; Irene, Amanda; Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT Update

Hi,

As you know, the SUPPORT papers were resubmitted to NEJM on 2/12. Wally received a request from Dr. Solomon yesterday stating the following:
I am writing again about your manuscript, "Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial." Your revision has been evaluated by the editors and addresses the key concerns raised previously. However, we do need to ask for some additional changes before it is accepted for publication. Revisions are being completed.

Neil received the following request:

Please send a copy of the revision in a Word (.doc) version to me via email at your soonest convenience.

We will keep folks updated as we here more. If you haven't sent your copyright form or ICMJE disclosure, please

do so asap.

Thanks

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Bell, Edward
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Wally Carlo
Subject: RE: CONFIDENTIAL: New England Journal of Medicine 09-11781.R1
Date: Saturday, February 20, 2010 9:41:00 AM

There's a typo on p. 21: "... we prospectively planned to evaluate this interactions..." It should be "interaction" (singular).

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 4:12 PM
Subject: CONFIDENTIAL: New England Journal of Medicine 09-11781.R1

Hi all, Here is the revised saturation paper.

Thanks to Wally for his quick turnaround!!!
Rose

From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: NEJM
Date: Friday, February 19, 2010 5:03:41 PM

Great news!

Congrats on a lot of work done

Carol

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, February 19, 2010 5:03 PM
To: Blaisdell, Carol (NIH/NHLBI) [E]
Subject: NEJM

Wally got the saturation paper back yesterday from NEJM with minor requests for revision. Neil was asked to send a word document so that the editor can do the track changes. Things are looking good!!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Bradley Yoder"
Subject: RE: SUPPORT SATURATION PAPER
Date: Friday, February 19, 2010 4:59:00 PM

YES
THNAKS
ROSE

From: Bradley Yoder [mailto:Bradley.Yoder@hsc.utah.edu]
Sent: Friday, February 19, 2010 4:57 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT SATURATION PAPER

Just checking to see if you received my fax.

Brad

Brad Yoder
Division of Neonatology
University of Utah SOM

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 6:54 AM
To: Bradley Yoder; 'Kristi Watterberg'; 'Finer, Neil'
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: SUPPORT SATURATION PAPER
Importance: High

We are missing the copyright form for the SUPPORT saturation paper. It is attached. Fill it out and either fax is to us (301-496-3790) or to the journal directly and let us know that it is done.

The title of the paper is:

**Oxygen Saturation Targets in Extremely Preterm Infants:
The SUPPORT Trial**

**The manuscript number is 09-11781
Waldemar A. Carlo is the corresponding author**

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Phelps, Dale"; "Michael O' Shea"; "Duara, Shahnaz"; "Finer, Neil"; "Rich, Wade"; "Anthony Piazza (Anthony.Piazza@oz.ped.emory.edu)"; "bsood@med.wayne.edu"; "Brenda Morris"; "Gantz, Marie"; "Laroya, Nirupama"; "Vivek Narendran"; "Poole Kenneth (E-mail)"; "Nancy Newman"; "(susie.buchter@oz.ped.emory.edu)"; "vineet.bhandari@yale.edu"; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; "Abhik Das"; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); "Brenda Poindexter"; "Carlo Waldemar (E-mail)"; cotte010@mc.duke.edu; "Dennis Wallace"; "Ed Bell"; "Ed Donovan"; "Ehrenkranz Richard (E-mail)"; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; "Kristi Watterberg"; Kurt Schibler (kurt.schibler@cchmc.org); "Matthew Bizzarro"; "Michelle Walsh"; "Mickey Caplan"; "Oh William (E-mail)"; "Pablo Sanchez"; "Poole Kenneth (E-mail)"; "Roger Faix"; "Ronald GOLDBERG"; "Seetha Shankaran"; "Stevenson David (E-mail)"; "Stoll Barbara (E-mail)"; "Tyson Jon (E-mail)"; VanMeurs, Krisa
Cc: "Zaterka-Baxter, Kristin"; "Cunningham, Meg"; "Carolyn Petrie"; "Newman, Jamie"; "Irene, Amanda"; Archer, Stephanie (NIH/NICHD) [E]
Subject: SUPPORT Update
Date: Friday, February 19, 2010 4:59:00 PM
Importance: High

Hi,

As you know, the SUPPORT papers were resubmitted to NEJM on 2/12. Wally received a request from Dr. Solomon yesterday stating the following:

I am writing again about your manuscript, "Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial." Your revision has been evaluated by the editors and addresses the key concerns raised previously. However, we do need to ask for some additional changes before it is accepted for publication. Revisions are being completed.

Neil received the following request:

Please send a copy of the revision in a Word (.doc) version to me via email at your soonest convenience.

We will keep folks updated as we here more. If you haven't sent your copyright form or ICMJE disclosure, please do so asap.

Thanks

Rose

Rosemary D. Higgins, MD

Program Scientist for the Neonatal Research Network

Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine

Eunice Kennedy Shriver National Institute of Child Health and Human Development

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301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Susan Hintz
To: Kris Zaterka
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: coming your way
Date: Friday, February 19, 2010 4:38:40 PM

Hi Kris

FYI - coming your way should be about 60-70 more completed SUPPORT MRI's. Erica is sending them out today...I think - or maybe on Monday. Also included in that pile is the MRI that Pat reviewed re: hydrocephalus for the hypothermia MRI study. He sent the revised scores by email as you know.

Thanks - after you get these and log them in, could you give me an updated number for SUPPORT MRI's. Actually, we should start referring to this subcohort as NEURO.

Also - I want to make sure that the supplementary MRI form is being entered in it's entirety - i.e., the second page with the individual scores (1-3) by individual white matter injury group, as well as the total score and the Miller classification. Correct?

Finally, I just got the other two MRI's by Fed Ex today. Next week I will bring those over to Pat as well during one of our usual early AM reading sessions

Thanks

susan

--

Susan R. Hintz, M.D., M.S. Epi
Associate Professor of Pediatrics
Division of Neonatal and Developmental Medicine
Stanford University School of Medicine
750 Welch Road, Suite 315
Palo Alto, CA 94304
ph: 650-723-5711
fax: 650-725-8351

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abel, Brendan"
Cc: "Wally Carlo, M.D."
Subject: RE: 09-11781
Date: Friday, February 19, 2010 4:29:00 PM
Attachments: ICMJE-Disclosure-Form-102309 support morris.pdf
ICMJE-Disclosure-Form-102309 support morris.pdf

Here are Dr. Morris's forms
Rose

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Friday, February 19, 2010 3:26 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: 'Wally Carlo, M.D.'
Subject: RE: 09-11781

Hi Rose,

Thanks for sending. Unfortunately, many of the disclosure forms are not filled out correctly. The majority will be a quick fix, but several others need to be filled out electronically.

Most of the forms are correctly filled out, but must be sent in the original pdf format. They should appear just like the attached form, where the form is still in its interactive format. This likely means you'll have to attach each form separately. Feel free to take as many emails as you need. My inbox is used to it. (This applies to Drs. Bell, Carlo, Cotten, Ehrenkrantz, Laptook, Narendran, Newman, O'Shea, Phelps, Piazza, Poindexter, Sanchez, and Sood.)

Drs. Duara, Faix, and Watterberg will need to fill out their forms electronically (rather than handwritten) and send in their original pdf format.

Dr. Gantz needs to complete Sec. 2- there should be two boxes checked in each row. He can see the attached sample for guidance.

Dr. Yoder just needs to choose Yes or No under the "To Your Institution" in consulting row.

The good news is that all copyright transfer forms appear complete.

Let me know if you have any questions. I'll be at my desk for the next hour or so. You're welcome to send at beginning of next week if you don't want to spend your Friday afternoon taking care of this.

Have a nice weekend,

Brendan

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 2:51 PM
To: Abel, Brendan
Cc: 'Wally Carlo, M.D.'
Subject: 09-11781

Hi Brendan,

In an effort to get the required copyright and ICMJE forms for the co-authors for manuscript 09-11781, I am attaching two pdf's which have many of the required forms. Dr. Ivan Franz will submit his forms directly to your office on Monday.

Would it be possible for you to let Wally or I know who is missing (if any)? We can assist the co-authors with completion of the forms.

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
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INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Given Name:
(or first)

Brenda

Surname:
(or last)

Morris

Effective Date: 04-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it): 09-11781

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funded trial	Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	NICHD/UT Houston	Expenses for travel	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

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(or first)

Brenda

Surname:
(or last)

Morris

Effective Date:

04-February-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it):

09-11781

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No

Yes, specify nature of compensation

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funded trial	Del x
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Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	NICHD/UT Houston	Expenses for travel	Del x
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							Add +
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							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

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							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

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MEDICAL JOURNAL EDITORS

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At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "babel@nejm.org"
Cc: "Wally Carlo, M.D."
Subject: 09-11781
Date: Friday, February 19, 2010 3:14:00 PM
Attachments: NEJM forms SUPPORT CARLO - POOLE.pdf

Brendan
Here is Dr. Poole's information

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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Contribution Number: 09-11781

Short Title or description of Contribution: Oxygen Saturation Targets SUPPORT Trial

Corresponding Author: Waldemar A. Carlo

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							Add +
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							Add +
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						Add +
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							Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
							Add +
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							Add +
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							Add +
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							Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
							Add +
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							Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
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Hi Brendan,

In an effort to get the required copyright and ICMJE forms for the co-authors for manuscript 09-11781, I am attaching two pdf's which have many of the required forms. Dr. Ivan Franz will submit his forms directly to your office on Monday.

Would it be possible for you to let Wally or I know who is missing (if any)? We can assist the co-authors with completion of the forms.

Thanks
Rose

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Pregnancy and Perinatology Branch
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
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						Add +
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						Add +
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						Add +
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						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	University of Iowa	The University reimburses, with funds from my NIH grant, my travel costs to attend the meetings of the NICHD Neonatal Research Network	Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Short Title or description of Contribution: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets In Extremely Premature Infants

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Corresponding Author: Waldemar A Carlo in extremely premature infants

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Corresponding author's name:

Waldemar A. Carlo

Manuscript Title:

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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Duke University	this was a multicenter trial sponsored by NICHD. The institution received capitation payment for study expenses, and a base award was provided to centers in the Network for study personnel and infrastructure.	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		As part of the base award, there is a portion of the overall budget set aside for travel to Network/ study steering committee meetings in the Washington D. C. area at the NIH rate.	Del x
							Add +

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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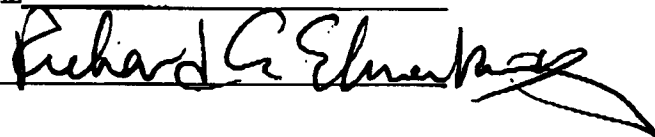
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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD	Salary support for research staff	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

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						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eunice Kennedy Shriver National Institute of Child Health and Human Development		Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Short Title or description of Contribution: Oxygen Saturation Targets: SUPPORT Trial

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	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del X
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Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del X



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment support at NICHD		Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			Del x
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						Add +
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Short Title or description of Contribution: Randomized Trial of Oxygen Saturation

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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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							Add +
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							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



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						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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Short Title or description of Contribution: The SUPPORT TRIAL RCT of O₂ saturations

Corresponding Author: Waldemar A. Carlo

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Effective Date: 27-January-2010

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Manuscript Identifying Number (if you know it):

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	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH - NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	for travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	grant supported working meetings	Del x
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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Short Title or description of Contribution: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Corresponding Author: Waldemar A. Carlo

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Corresponding author's name: Waldemar A. Carlo

Manuscript Title: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

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Yes, specify nature of compensation

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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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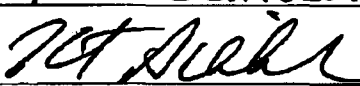
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Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		



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Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Study Oximeters Provided by Neonatal Network
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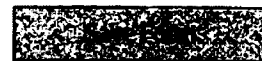
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							Add +
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							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
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							Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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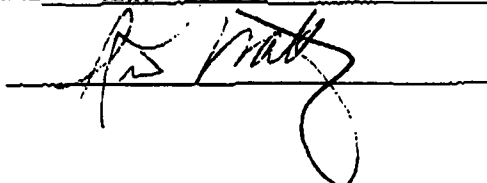
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								Add +
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								Add +
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								Add +
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							Add +
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							Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Del x
							Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Del x
							Add +
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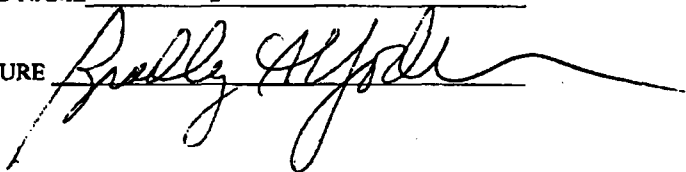
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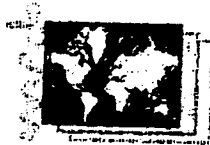
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Corresponding Author: Wally Carlo in Emergency Practice Unit

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Wally Carlo

Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets In Extremely Premature Infants

Manuscript Identifying Number (if you know it):

09-11781

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						Add +
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						Add +
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						Add +
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						Add +
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						Add +
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Short Title or description of Contribution: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Corresponding Author: Waldemar A. Carlo

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Corresponding author's name: Waldemar A. Carlo

Manuscript Title: Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

Manuscript Identifying Number (if you know it): 09-11781

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						Add +
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						Add +
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						Add +
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						Add +
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Waldemar Carlo, MD

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Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Cincinnati Site Principal Investigator to attend Steering Committee Meeting
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Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH NICHD Neonatal Research Network	HD027853 - Study Oximeters Provided by Neonatal Network
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Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		



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Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		

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Manuscript Title:

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							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
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							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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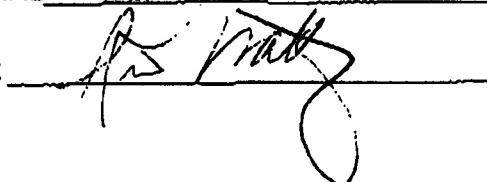
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					NICHD				
Grant	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	NEONATAL RESEARCH NETWORK	Del x
									Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
									Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
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Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
									Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
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Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Del x
								Add +
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									Add +
Royalties	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
Stock/stock options	<input checked="" type="checkbox"/>		<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				Del x
									Add +
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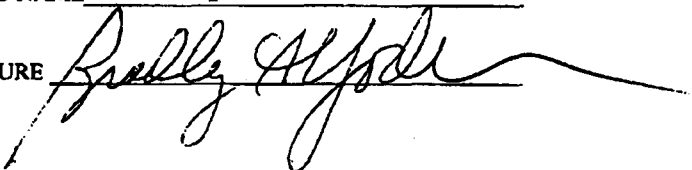
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							Add +
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						Add +
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						Add +
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						Add +
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						Add +
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						Add +
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						Add +
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						Add +
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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Duke University	this was a multicenter trial sponsored by NICHD. The institution received capitation payment for study expenses, and a base award was provided to centers in the Network for study personnel and infrastructure.	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		As part of the base award, there is a portion of the overall budget set aside for travel to Network/study steering committee meetings in the Washington D. C. area at the NIH rate.	Del x
							Add +

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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x

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Type of Relationship (In alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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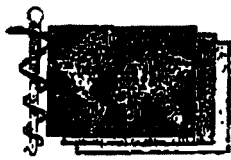
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board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (ext on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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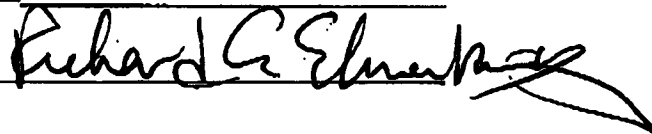
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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH/NICHD	Salary support for research staff	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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Yes, specify nature of compensation NICHD Grant #U10 MD 053124

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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (In alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

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 Yes, the following relationships/conditions/circumstances are present (explain below):

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Manuscript Title:

The SUPPORT Trial: Randomized Trial of Oxygen
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Waldemar A. Carlo

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	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Eunice Kennedy Shriver National Institute of Child Health and Human Development		Del x
							Add +
Consulting fee or honorarium	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
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						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

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Contribution Number: 09-11761

Short Title or description of Contribution: Oxygen Saturation Targets: SUPPORT Trial

Author: Waldemar D'10

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Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del x
							Add +
Payment for writing or reviewing the manuscript	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment at NICHD		Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	As part of employment support at NICHD		Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>			Del x
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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Employee and Program Scientist	Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
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Short Title or description of Contribution: Randomized Trial of Oxygen Saturation

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Corresponding author's name:

Wally Carlo MD

Manuscript Title:

The Support Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

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No

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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						Add +
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						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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Short Title or description of Contribution: CINCINNATI CENTER PI/CO-PI
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Narendran

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Are you the corresponding author? Yes No

Manuscript Title: The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Manuscript Identifying Number (if you know it): 09-11783

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						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

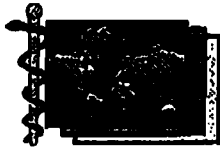


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						Add +
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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
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						Add +
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Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
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Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
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Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD grant	U10 HD40498, GCRC M01 RR7122	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
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Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
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						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x



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						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
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Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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781.207.6529 FAX**

Contribution Number: 09-11781

Short Title or description of Contribution: The SUPPORT TRIAL RCT of O₂ saturations

Corresponding Author: Waldemar A. Carlo

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If author was a U.S. Government employee at the time the article was written, please check below.

AGREED TO THIS DAY OF JAN 27, 2010

()

PRINTED NAME Dale L Phelps, MD

SIGNATURE Dale L Phelps, MD



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Section 1. Identifying Information.

Given Name:
(or first)

Dale

Surname:
(or last)

Phelps

Effective Date:

27-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

The SUPPORT Trial: Randomized trial of oxygen saturation targets in extremely premature infants

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NIH - NICHD	Neonatal Research Network	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	for travel to working meetings	Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NIH - NICHD	grant supported working meetings	Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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From: [Kristi Watterberg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT SATURATION PAPER
Date: Friday, February 19, 2010 11:54:02 AM

apologies - don't know what happened ~ Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/19/2010 9:52 AM >>>
Kristi

We did not get the copy right form - sorry for the trouble. We also need it for Neil's paper.

Rose

From: Kristi Watterberg [<mailto:KWatterberg@salud.unm.edu>]
Sent: Friday, February 19, 2010 11:42 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT SATURATION PAPER

I will do so today, but I did send both of them together to you when previously requested. - Kristi

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/19/2010 6:53 AM >>>

We are missing the copyright form for the SUPPORT saturation paper. It is attached. Fill it out and either fax is to us (301-496-3790) or to the journal directly and let us know that it is done.

The title of the paper is:

Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial

The manuscript number is 09-11781

Waldemar A. Carlo is the corresponding author

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health

6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: ["Krisa Van Meurs"](#)
Cc: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Subject: SUPPORT PAPERS
Date: Friday, February 19, 2010 11:53:00 AM

Krisa

Did you submit your ICMJE form on-line for the SUPORT papers?

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT SATURATION PAPER
Date: Friday, February 19, 2010 11:50:45 AM

Only got the copyright form, not the ICMJE.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430
Fax 301-496-3790
archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Friday, February 19, 2010 11:50 AM
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: SUPPORT SATURATION PAPER

??

From: Kristi Watterberg [mailto:KWatterberg@salud.unm.edu]
Sent: Friday, February 19, 2010 11:42 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: SUPPORT SATURATION PAPER

I will do so today, but I did send both of them together to you when previously requested. - Kristi

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Waldemar A. Carlo is the corresponding author

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Friday, February 19, 2010 10:19 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT SATURATION PAPER

Rose

I will call you this morning RE Susans abstract Reference List

Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 5:54 AM
To: Brad Yoder (Bradley.yoder@hsc.utah.edu); 'Kristi Watterberg'; Finer, Neil
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: SUPPORT SATURATION PAPER
Importance: High

We are missing the copyright form for the SUPPORT saturation paper. It is attached. Fill it out and either fax is to us (301-496-3790) or to the journal directly and let us know that it is done.

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**The manuscript number is 09-11781
Waldemar A. Carlo is the corresponding author**

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
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MSC 7510

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301-496-3790 (FAX)
higginsr@mail.nih.gov

From: [Sood, Beena](#)
To: [Archer, Stephanie \(NIH/NICHD\) \[E\]](#)
Cc: wacarlo@uab.edu; [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: Request for forms for saturation SUPPORT paper
Date: Friday, February 19, 2010 10:18:03 AM
Attachments: [ICMJE-Disclosure-Form-102309_NCPAP.pdf](#)
[ICMJE-Disclosure-Form-102309_SpO2.pdf](#)
[NEJM-CTA-2009_NCPAP_Scanned.pdf](#)
[NEJM-CTA-2009_SpO2_Scanned.pdf](#)

Stephanie,

I am attaching my materials – let me know if this format is acceptable for submission – if needed I can also submit directly online

I am also attaching the corresponding materials for the NCPAP paper

Thanks

Beena

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, February 19, 2010 8:52 AM
To: Abhik Das; Sood, Beena; 'Brenda Poindexter'; Brenda Morris; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Gantz, Marie; Laroia, Nirupama; 'Michael O` Shea'; 'Poole Kenneth (E-mail)'; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: Request for forms for saturation SUPPORT paper
Importance: High

Hi,

We are missing forms for the saturation paper from you.

Please fill out the attached copyright and disclosure form.

You may either submit them on line or fax them to us (301-496-3790). Please do this *TODAY!!!!*

Let me know if there are any questions.

The title of the paper is:

**Oxygen Saturation Targets in Extremely Preterm Infants:
The SUPPORT Trial**

The manuscript number is 09-11781

Waldemar A. Carlo is the corresponding author

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch

Center for Developmental Biology and Perinatal Medicine
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2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Section 1. Identifying Information.

Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funding for study	Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



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The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Section 1. Identifying Information.

Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	NICHD	Funding for study	Del x
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	NICHD	Travel to PI Meetings	Del x
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x



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Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
							Add +
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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Contribution Number: 09-11783
Short Title or description of Contribution: Early CPAP versus Surfactant and outcomes of prematurity
Corresponding Author: Neil N. Finer, MD

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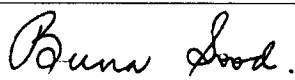
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PRINTED NAME Beena G. Sood, MD, MS

SIGNATURE 

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Contribution Number: 09-11781
Short Title or description of Contribution: Oxygen saturation and outcomes of prematurity
Corresponding Author: Waldemar A. Carlo, MD

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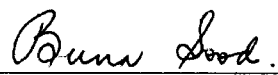
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(_____)

PRINTED NAME Beena G. Sood, MD, MS

SIGNATURE 

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Gantz, Marie"
Cc: "Das, Abhik"; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: Request for forms for saturation SUPPORT paper
Date: Friday, February 19, 2010 9:55:00 AM

Great
Thanks
Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Friday, February 19, 2010 9:24 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: RE: Request for forms for saturation SUPPORT paper

When I asked him if he faxed his forms directly to the journal he said he couldn't remember, which I took to mean that he had already taken care of it by sending the forms either to you or to NEJM but he could not remember which.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-8255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 9:22 AM
To: Gantz, Marie
Cc: Das, Abhik; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: Request for forms for saturation SUPPORT paper

Not necessary – did Abhik send his also?
Thanks
Rose

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Friday, February 19, 2010 9:22 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: RE: Request for forms for saturation SUPPORT paper

I faxed my forms directly to the journal a while back (per instructions on the form), but I will fax them to you as well.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International

mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 19, 2010 8:52 AM
To: Das, Abhik; bsood@med.wayne.edu; 'Brenda Poindexter'; Brenda Morris; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Gantz, Marie; Laroia, Nirupama; 'Michael O`Shea'; Poole, W. Kenneth; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: Request for forms for saturation SUPPORT paper
Importance: High

Hi,

**We are missing forms for the saturation paper from you.
Please fill out the attached copyright and disclosure form.
You may either submit them on line or fax them to us (301-496-3790). Please do this *TODAY!!!!***

Let me know if there are any questions.

The title of the paper is:

**Oxygen Saturation Targets in Extremely Preterm Infants:
The SUPPORT Trial**

**The manuscript number is 09-11781
Waldemar A. Carlo is the corresponding author**

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: FW: New England Journal of Medicine 09-11781
Date: Friday, February 19, 2010 9:29:00 AM
Attachments: Rich ICMJE-Disclosure-Form.pdf
Rich ICMJE-Disclosure-Form-102309 (CPAP).pdf

-----Original Message-----

From: Rich, Wade [mailto:wrich@ucsd.edu]
Sent: Friday, February 19, 2010 9:29 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: New England Journal of Medicine 09-11781

I sent them directly to Brendan at his request.
wade

-----Original Message-----

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Friday, February 12, 2010 7:21 AM
To: Rich, Wade
Subject: RE: New England Journal of Medicine 09-11781

Great. Just want to confirm that "No" down section 3 is also correct (as attached). Assuming ok, you're all set.

Thanks,

Brendan

-----Original Message-----

From: Rich, Wade [mailto:wrich@ucsd.edu]
Sent: Friday, February 12, 2010 10:17 AM
To: Abel, Brendan
Subject: RE: New England Journal of Medicine 09-11781

Both corrected FDs.
Wade

-----Original Message-----

From: onbehalf+f+babel+nejm.org@manuscriptcentral.com
[mailto:onbehalf+f+babel+nejm.org@manuscriptcentral.com] On Behalf Of babel@nejm.org
Sent: Friday, February 12, 2010 7:01 AM
To: Rich, Wade
Subject: New England Journal of Medicine 09-11781

Re: 09-11781 - The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Dear Mr. Rich:

Thanks for sending in your copyright transfer and financial disclosure forms. Both CTAs are good as is. Please email the financial disclosure form to me in its original pdf format. It appears that you've filled out correctly for the most part. However, I was wondering why you chose "Yes" at the top of Part 2, but then never selected any type of support. If you haven't received any, just click no. If you have, then please clarify on the form.

Thanks,

Brendan

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
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INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Section 1. Identifying Information.

Given Name: Surname: Effective Date:

Format example: 07-August-2008

Are you the corresponding author? Yes No

Corresponding author's name:

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

- No
- Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +

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Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
 Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
 Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

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INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



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Surname:
(or last)

Effective Date:

Format example: 07-August-2008

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Corresponding author's name:

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Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Rich, Wade"
Subject: RE: New England Journal of Medicine 09-11781
Date: Friday, February 19, 2010 9:29:00 AM

Awesome
Thanks
rose

-----Original Message-----

From: Rich, Wade [mailto:wrich@ucsd.edu]
Sent: Friday, February 19, 2010 9:29 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: New England Journal of Medicine 09-11781

I sent them directly to Brendan at his request.
wade

-----Original Message-----

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Friday, February 12, 2010 7:21 AM
To: Rich, Wade
Subject: RE: New England Journal of Medicine 09-11781

Great. Just want to confirm that "No" down section 3 is also correct (as attached). Assuming ok, you're all set.

Thanks,

Brendan

-----Original Message-----

From: Rich, Wade [mailto:wrich@ucsd.edu]
Sent: Friday, February 12, 2010 10:17 AM
To: Abel, Brendan
Subject: RE: New England Journal of Medicine 09-11781

Both corrected FDs.
Wade

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com] On Behalf Of babel@nejm.org
Sent: Friday, February 12, 2010 7:01 AM
To: Rich, Wade
Subject: New England Journal of Medicine 09-11781

Re: 09-11781 - The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Dear Mr. Rich:

Thanks for sending in your copyright transfer and financial disclosure forms. Both CTAs are good as is. Please email the financial disclosure form to me in its original pdf format. It appears that you've filled out correctly for the most part. However, I was wondering why you chose "Yes" at the top of Part 2, but then never selected any type of support. If you haven't received any, just click no. If you have, then please clarify on the form.

Thanks,

Brendan

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Wally Carlo, M.D."
Subject: RE: Request for forms for saturation SUPPORT paper
Date: Friday, February 19, 2010 8:55:00 AM

Now to the actual questions you sent me!!

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Friday, February 19, 2010 8:55 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Request for forms for saturation SUPPORT paper

THANKS!!

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Fri 2/19/2010 7:52 AM
To: Abhik Das; bsood@med.wayne.edu; 'Brenda Poindexter'; Brenda Morris; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Gantz, Marie; Laroia, Nirupama; 'Michael O`Shea'; 'Poole Kenneth (E-mail)'; Rich, Wade
Cc: Archer, Stephanie (NIH/NICHD) [E]; wacarlo@uab.edu
Subject: Request for forms for saturation SUPPORT paper

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**We are missing forms for the saturation paper from you.
Please fill out the attached copyright and disclosure form.
You may either submit them on line or fax them to us (301-496-3790). Please do this *TODAY!!!!***

Let me know if there are any questions.

The title of the paper is:

**Oxygen Saturation Targets in Extremely Preterm Infants:
The SUPPORT Trial**

**The manuscript number is 09-11781
Waldemar A. Carlo is the corresponding author**

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892

For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Brad Yoder (Bradley.yoder@hsc.utah.edu)"; "Kristi Watterberg"; "Finer, Neil"
Cc: Archer, Stephanie (NIH/NICHD) [E]; "wacarlo@uab.edu"
Subject: SUPPORT SATURATION PAPER
Date: Friday, February 19, 2010 8:53:00 AM
Attachments: NEJM-CTA-2009.pdf
Importance: High

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The title of the paper is:

**Oxygen Saturation Targets in Extremely Preterm Infants:
The SUPPORT Trial**

**The manuscript number is 09-11781
Waldemar A. Carlo is the corresponding author**

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
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To: "Abhik Das"; "bsood@med.wayne.edu"; "Brenda Poindexter"; "Brenda Morris"; "Ivan Frantz (ifrantz@tuftsmedicalcenter.org)"; "Gantz, Marie"; "Laroia, Nirupama"; "Michael O' Shea"; "Poole Kenneth (E-mail)"; "Rich, Wade"
Cc: Archer, Stephanie (NIH/NICHD) [E]; "wacar10@uab.edu"
Subject: Request for forms for saturation SUPPORT paper
Date: Friday, February 19, 2010 8:52:00 AM
Attachments: [_NEJM-inst-for-ICMJE-form.pdf](#)
[_NEJM-CTA-2009.pdf](#)
[_ICMJE-Disclosure-Form-102309.pdf](#)
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Are you the corresponding author? Yes No

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

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If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

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						Add
Consultancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del
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Employment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del
						Add
Expert testimony	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add



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INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Gifts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Honoraria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
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						Add +
Patents (planned, pending or issued)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Royalties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Payment for development of educational presentations including service on speakers' bureaus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Stock/stock options	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Travel/accommodations expenses covered or reimbursed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Other (err on the side of full disclosure)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



ICMJE

INTERNATIONAL COMMITTEE *of*
MEDICAL JOURNAL EDITORS

ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Thursday, February 18, 2010 7:15 PM
To: Wally Carlo, M.D.; Higgins, Rosemary (NIH/NICHD) [E]
Cc: das@rti.org; Gantz, Marie; Rich, Wade
Subject: RE: New England Journal of Medicine 09-11781.R1

Great news Wally
These changes all look fine to me
God bless Ola
Neil

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, February 18, 2010 3:22 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Finer, Neil; das@rti.org; Gantz, Marie; Rich, Wade
Subject: FW: New England Journal of Medicine 09-11781.R1

Hi Everyone:

Great news!!! Sorry for the delay. I have been in the NICU.

They are doing this fast!! They want them published soon, I think. I will work on this tonight.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: onbehalfof+editorial+nejm.org@manuscriptcentral.com
[mailto:onbehalfof+editorial+nejm.org@manuscriptcentral.com] On Behalf Of editorial@nejm.org
Sent: Thursday, February 18, 2010 2:52 PM
To: Wally Carlo, M.D.
Subject: New England Journal of Medicine 09-11781.R1

Dear Wally:

I am writing again about your manuscript, "Oxygen Saturation Targets in Extremely Preterm Infants: The SUPPORT Trial." Your revision has been evaluated by the editors and addresses the key concerns raised previously. However, we do need to ask for some additional changes before it is accepted for publication.

At this point I am attaching a partially edited version of your manuscript in which I have inserted editorial comments and queries.

(These comments are most easily viewed in Word by viewing in "reading layout" or "print layout.") In general, the changes I have suggested should be incorporated, unless there are places where I have inadvertently changed your meaning.

When you send in your revised manuscript, it is not necessary to provide a letter with responses to the inserted editorial comments, but please note anywhere that you did not make suggested changes (and why); it is fine to insert any responses in the associated comment box. Please return two copies of the revision: one in which the changes you have made are highlighted, and the other a clean copy.

Please include a word count for the text. As you know, the word count for text should not exceed 2700 words, and there should be no more than 5 tables or figures in the print version of the manuscript, though it is fine to include additional "web only" appendix tables.

Any changes in authorship must be made in writing, signed by all authors.

To revise your manuscript, log into <http://mc.manuscriptcentral.com/nejm> and enter For Authors, where you will find a button to "Submit a Revision."

Journal policy dictates that we must have on file a signed Copyright Transfer Agreement from each author before a manuscript can be accepted.

If not already done, please ask all authors to sign and fax back the enclosed form as soon as possible to (781) 207-6529. This will eliminate unnecessary delays in the event that your manuscript is accepted.

The Universal Disclosure form is also attached. Each author must complete it. After you have filled in the appropriate information in the spaces provided, you may either e-mail your completed form to Brendan Abel at babel@nejm.org or upload it to your Author Dashboard of ScholarOne Manuscripts. It is essential that you return the forms as soon as possible, because we cannot process your manuscript without them.

Please recall that the Journal requires that neither an article under consideration nor any part of its essential substance, tables, or figures has been or will be published or submitted elsewhere before appearing in the Journal.

We look forward to receiving your revised manuscript and will plan a prompt evaluation when it arrives. Please do not hesitate to contact me if you have questions.

Thank you again for your work.

Sincerely,

Caren Solomon

Caren G. Solomon, MD
Deputy Editor

New England Journal of Medicine
10 Shattuck Street
Boston, MA 02115
(617) 734-9800
Fax: (617) 739-9864
<http://www.nejm.org>

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wcarlo@peds.uab.edu"
Cc: "nfiner@ucsd.edu"; "das@rti.org"; "mgantz@rti.org"; "wrich@ucsd.edu"
Subject: Re: New England Journal of Medicine 09-11781.R1
Date: Thursday, February 18, 2010 6:41:18 PM

Great!!!!

----- Original Message -----

From: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: nfiner@ucsd.edu <nfiner@ucsd.edu>; das@rti.org <das@rti.org>; Gantz, Marie <mgantz@rti.org>; wrich@ucsd.edu <wrich@ucsd.edu>
Sent: Thu Feb 18 18:21:35 2010
Subject: FW: New England Journal of Medicine 09-11781.R1

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They are doing this fast!! They want them published soon, I think. I will work on this tonight.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: onbehalfof+editorial+nejm.org@manuscriptcentral.com
[mailto:onbehalfof+editorial+nejm.org@manuscriptcentral.com] On Behalf
Of editorial@nejm.org
Sent: Thursday, February 18, 2010 2:52 PM
To: Wally Carlo, M.D.
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(These comments are most easily viewed in Word by viewing in "reading layout" or "print layout.") In general, the changes I have suggested should be incorporated, unless there are places where I have inadvertently changed your meaning.

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Please include a word count for the text. As you know, the word count for text should not exceed 2700 words, and there should be no more than 5 tables or figures in the print version of the manuscript, though it is fine to include additional "web only" appendix tables.

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Please recall that the Journal requires that neither an article under consideration nor any part of its essential substance, tables, or figures has been or will be published or submitted elsewhere before appearing in the Journal.

We look forward to receiving your revised manuscript and will plan a prompt evaluation when it arrives. Please do not hesitate to contact me if you have questions.

Thank you again for your work.

Sincerely,

Caren Solomon

Caren G. Solomon, MD

Deputy Editor

New England Journal of Medicine

10 Shattuck Street

Boston, MA 02115

(617) 734-9800

Fax: (617) 739-9864

<http://www.nejm.org>

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"; "Abhik Das"; "Gantz, Marie"; "Carlo Waldemar (E-mail)"
Cc: "Rich, Wade"
Subject: RE: New England Journal of Medicine 09-11783.R1
Date: Thursday, February 18, 2010 4:49:00 PM

This means they want to do "track changes" on the word document!!!! A most awesome sign!!

-----Original Message-----

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Thursday, February 18, 2010 3:58 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Abhik Das; Gantz, Marie; Carlo Waldemar (E-mail)
Cc: Rich, Wade
Subject: FW: New England Journal of Medicine 09-11783.R1

Hi Everyone

I just got this request from the NEJM - and responded with this email

Lets hope it's all for the good

Wally did you get a similar request??

Neil

-----Original Message-----

From: Finer, Neil
Sent: Thursday, February 18, 2010 12:56 PM
To: 'babel@nejm.org'
Subject: RE: New England Journal of Medicine 09-11783.R1

Hello Brendan

I have attached the final submitted version and the Tables and Figure as WORD.docs - using Word 2004.

Let me know if these are OK

Regards

Neil Finer

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[\[mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com\]](mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com) On Behalf Of babel@nejm.org
Sent: Thursday, February 18, 2010 11:34 AM
To: Finer, Neil
Subject: New England Journal of Medicine 09-11783.R1

Re: 09-11783.R1 - Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Dear Dr. Finer:

Please send a copy of the revision in a Word (.doc) version to me via email at your soonest convenience.

Thank you.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Thursday, February 18, 2010 4:00 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Abhik Das; Carlo Waldemar (E-mail); Gantz, Marie
Cc: Rich, Wade
Subject: FW: New England Journal of Medicine 09-11783.R1

And the reply!!

Neil

-----Original Message-----

From: Abel, Brendan [mailto:babel@nejm.org]
Sent: Thursday, February 18, 2010 12:55 PM
To: Finer, Neil
Subject: RE: New England Journal of Medicine 09-11783.R1

They are great. I'll pass along to Dr. Solomon. We should be back in touch shortly.

Thanks,

Brendan

-----Original Message-----

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Thursday, February 18, 2010 3:56 PM
To: Abel, Brendan
Subject: RE: New England Journal of Medicine 09-11783.R1

Hello Brendan

I have attached the final submitted version and the Tables and Figure as WORD.docs - using Word 2004.

Let me know if these are OK

Regards

Neil Finer

-----Original Message-----

From: onbehalf+babel+nejm.org@manuscriptcentral.com
[mailto:onbehalf+babel+nejm.org@manuscriptcentral.com] On Behalf Of babel@nejm.org
Sent: Thursday, February 18, 2010 11:34 AM
To: Finer, Neil
Subject: New England Journal of Medicine 09-11783.R1

Re: 09-11783.R1 - Early CPAP versus Surfactant in Extremely Preterm Infants: The SUPPORT Trial

Dear Dr. Finer:

Please send a copy of the revision in a Word (.doc) version to me via email at your soonest convenience.

Thank you.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

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From: [Wallace, Dennis](#)
To: [Kristi Watterberg](#); [Zaterka-Baxter, Kristin](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT data
Date: Wednesday, February 17, 2010 6:02:57 PM

Kris,

I don't know whether Kris got back to you, but Marie indicated that she can pull the data together next week. Does that work?

Dennis

Dennis Wallace
Senior Research Statistician
Cox 241
RTI International
3040 Cornwallis Rd
Research Triangle Park, NC 27709-2104
Voice: 919-541-6271
Fax: 919-541-6416

From: [Kristi Watterberg \[mailto:KWatterberg@salud.unm.edu\]](mailto:KWatterberg@salud.unm.edu)
Sent: Wednesday, February 17, 2010 12:08 PM
To: [Wallace, Dennis](#); [Zaterka-Baxter, Kristin](#)
Cc: [Rosemary \(NIH/NICHD\) Higgins](#)
Subject: Fwd: SUPPORT data

Hi, Dennis and Kris - I got an out of office message from Abhik saying he'll be gone until March 6. Would it be possible to get the data described in the e-mail before then? thanks, Kristi

From: [Kristi Watterberg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: RE: SUPPORT data
Date: Wednesday, February 17, 2010 3:11:13 PM

thanks!

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/17/2010 10:10 AM >>>

It is fine for Marie to do this - the SUPPORT subcommittee approved it and it is part of Michel's BPD secondary study.

Rose

From: Kristi Watterberg [<mailto:KWatterberg@salud.unm.edu>]
Sent: Wednesday, February 17, 2010 12:08 PM
To: Dennis Wallace; kzaterka@rti.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Fwd: SUPPORT data

Hi, Dennis and Kris - I got an out of office message from Abhik saying he'll be gone until March 6. Would it be possible to get the data described in the e-mail before then? thanks, Kristi

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"; wacarlo@uab.edu
Subject: SUPPORT
Date: Wednesday, February 17, 2010 12:40:00 PM

Hi,
There was interest in discussing the SUPPORT trial results on the SC call this coming week. I will put this on the agenda for 330 PM on 2/23. Neil – can you join?

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852.
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Kristi Watterberg"; "Dennis Wallace"; "kzaterka@rti.org"
Subject: RE: SUPPORT data
Date: Wednesday, February 17, 2010 12:10:00 PM

It is fine for Marie to do this – the SUPPORT subcommittee approved it and it is part of Michel's BPD secondary study.

Rose

From: Kristi Watterberg [mailto:KWatterberg@salud.unm.edu]
Sent: Wednesday, February 17, 2010 12:08 PM
To: Dennis Wallace; kzaterka@rti.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Fwd: SUPPORT data

Hi, Dennis and Kris - I got an out of office message from Abhik saying he'll be gone until March 6. Would it be possible to get the data described in the e-mail before then? thanks, Kristi

From: [Kristi Watterberg](#)
To: [Dennis Wallace; kzaterka@rti.org](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Fwd: SUPPORT data
Date: Wednesday, February 17, 2010 12:08:29 PM
Attachments: [SUPPORT data.msg](#)

Hi, Dennis and Kris - I got an out of office message from Abhik saying he'll be gone until March 6. Would it be possible to get the data described in the e-mail before then? thanks, Kristi

Blansfield, Earl (NIH/NICHD) [E]

From: Kristi Watterberg <KWatterberg@salud.unm.edu>
Sent: Wednesday, February 17, 2010 12:01 PM
To: adas@rti.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT data

Hi, Abhik - I understand that the SUPPORT subcommittee OK'd giving the hydrocortisone protocol development group the data regarding the BPD/death outcomes for SUPPORT babies still on ETT/ventilation at 14 days. Can you also let me know the % of the SUPPORT babies who were still on IMV at 14 days? I'd like to have that information if possible before the next subcommittee meeting, scheduled for March 1.

thanks! Kristi

From: Susan Hintz
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Re: neuroimaging
Date: Wednesday, February 17, 2010 8:30:14 AM

Hi Rose

Yes, I have met him, and Pat knows him. Thanks for the heads up. I will let you know if I hear from him.

Susan

Sent from my iPhone

On Feb 16, 2010, at 12:46 PM, "Higgins, Rosemary (NIH/NICHD) [E]"
<higginsr@mail.nih.gov> wrote:

Susan

Ashok Panigrahy M.D. had contacted me about neuroimaging in the NRN. He is interested in imaging at older ages. He told me that he had given a talk at Stanford and met you. He wanted to know how proposals worked for the NRN. He is interested in imaging children at 10 years of age – this is uncharted territory for the NRN. I told him you were running the large SUPPORT NEUROIMAGING TUDY

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health
6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Finer, Neil"; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; "Abhik Das"; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); "Brenda Poindexter"; "Carlo Waldemar (E-mail)"; cotte010@mc.duke.edu; "Dennis Wallace"; "Ed Bell"; "Ed Donovan"; "Ehrenkranz Richard (E-mail)"; Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; "Kristi Watterberg"; Kurt Schibler [kurt.schibler@cchmc.org]; "Matthew Bizzarro"; "Michelle Walsh"; "Mickey Caplan"; "Oh William (E-mail)"; "Pablo Sanchez"; "Poole Kenneth (E-mail)"; "Roger Faix"; "Ronald GOLDBERG"; "Seetha Shankaran"; "Stevenson David (E-mail)"; "Stoll Barbara (E-mail)"; "Tyson Jon (E-mail)"; VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; "Zaterka-Baxter, Kristin"; "Newman, Jamie"
Subject: Breathing Outcomes - prelim data request
Date: Tuesday, February 16, 2010 4:43:00 PM
Attachments: Breathing Outcomes - prelim data request.doc

Hi,

Tim Stevens is preparing a revision to his school age breathing outcomes study protocol and would like the following information from the school age SUPPORT trial for the 6 and 12 month visits.

Please let me know by February 23 if the data can be given at this time. Some of the infants have not yet completed the 12 month assessment.

Thanks
Rose

Since our last contact with you about your child.....

8. How many times has your child stayed in the hospital for one or more nights in a row? |__|__| times

8a. How many of these times were because of wheezing or breathing problems? |__|__| times

9. Since our last contact with you, has your baby's chest sounded wheezy or whistling?

1 Yes 2 No 3 Don't Know *Ask Question 9a for all responses*

9a. "Has your baby's breathing sounded like this?" (*play audio clip of wheezing*).

1 Yes 2 No 3 Don't Know

9f. Since our last contact with you, during the worst 2 week period, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say... (f.1)

- 1 Never
- 2 Twice a week or less
- 3 More than two times a week, but not every day
- 4 Everyday, but *not* all the time
- 5 Everyday, all the time

The Nighttime? Would you say... (f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a week/Frequently

10. Since our last contact with you, has your child had a cough for more than 3 days when he/she did not have a cold?

1 Yes 2 No *If NO, skip to Question 11*

IF YES TO QUESTION 10

10a. At what time of the day has this cough usually occurred?

(CHECK ALL THAT APPLY)

- 1 In the morning, shortly after rising
- 2 Later in the day
- 3 During the night
- 4 No relation to time of day

10f. Since our last contact with you, during the worst 2-week period, how often has your child had coughing?

The Daytime? Would you say... (f.1)

- 1 Never
- 2 Twice a week or less
- 3 More than two times a week, but not every day
- 4 Everyday, but *not* all the time
- 5 Everyday, all the time

The Nighttime? Would you say... (f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a week/Frequently

MEDICATIONS (Enter responses in table. Do not prompt for each medication in the Medication Code List below.)

The last two questions involve the medicines your child is taking for breathing problems.

27. Since our last contact with you, what medicines has your baby taken, including medicines delivered by a nebulizer or breathing machine at home?	27a. Code	27b. Does he/she take that medicine everyday, sometimes or only when sick? (repeat for each medication)
1		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
2		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
3		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
4		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
5		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
6		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
7		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick

Medication Code List:

<p>Rescue medicines: 1 Albuterol 2 Proventil 3 Serevent 4 Ventolin 5 Volmax 6 Xopenex</p> <p>Other Inhaled medications: 7 Cromolyn (Intal) 8 Nedocromil (Tilade)</p> <p>Inhaled steroids: 9 Advair 10 Aerobid 11 Azmacort 12 Beclovent 13 Flovent 14 Vanceril 15 Pulmicort</p>	<p>Systemic steroids: 16 Decadron 17 Prednisone 18 Prednisolone</p> <p>Leukotriene blocker: 19 Accolate 20 Singulair</p> <p>Methylxanthines: 21 Theophylline</p> <p>Diuretic medications: 22 Diuril 23 Lasix 24 Aldactizide 25 Aldactone</p> <p>Miscellaneous / Non-specific 26 Nebulizer 27 Other _____</p>
--	---

From: Stevens, Timothy
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: School Age Breathing Outcomes
Date: Tuesday, February 16, 2010 1:35:57 PM
Attachments: Breathing Outcomes - prelim data request.doc

Hi Rose

The 2 page word document is attached. Did that come through properly to you?

Thanks

Tim

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 16, 2010 1:07 PM
To: Stevens, Timothy
Subject: RE: School Age Breathing Outcomes

Tim,

Question 27 is not on the list – can you resend a word document with all the questions so I can send it to the steering committee?

THNAKS

ROSE

From: Stevens, Timothy [mailto:Timothy_Stevens@URMC.Rochester.edu]
Sent: Sunday, February 14, 2010 4:03 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: School Age Breathing Outcomes

Hi Rose,

As you know, one of the criticisms of the School Age Breathing Outcomes Proposal is the lack of preliminary data from Breathing Outcomes that supports longer term follow up. To address this concern Richard and I thought it would be helpful to have preliminary analyses of a few questions from Breathing Outcomes.

Here are selections from the 6 and 12 month Breathing Outcome questionnaires (questions #8, 9, 9a, 9f, 10, 10f and 27) that look at health care utilization, respiratory symptoms and medication use. Hopefully, analysis of the responses to these questions will provide data to further support school age follow-up.

Thanks

Tim

Since our last contact with you about your child.....

8. How many times has your child stayed in the hospital for one or more nights in a row? times

8a. How many of these times were because of wheezing or breathing problems? times

9. Since our last contact with you, has your baby's chest sounded wheezy or whistling?

1~ Yes 2~ No 3~ Don't Know Ask Question 9a for all responses

9a. "Has your baby's breathing sounded like this?" (*play audio clip of wheezing*).

1~ Yes 2~ No 3~ Don't Know

9f. Since our last contact with you, during the worst 2 week period, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say... (f.1)

- 1 Never
- 2 Twice a week or less
- 3 More than two times a week, but not every day
- 4 Everyday, but *not* all the time
- 5 Everyday, all the time

week/Frequently

The Nighttime? Would you say...(f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a

10. Since our last contact with you, has your child had a cough for more than 3 days when he/she did not have a cold?

1 ~ Yes 2 ~ No *If NO, skip to Question 11*

10f. Since our last contact with you, during the worst 2-week period, how often has your child had coughing?

The Daytime? Would you say... (f.1)

- 1 Never
- 2 Twice a week or less
- 3 More than two times a week, but not every day
- 4 Everyday, but *not* all the time
- 5 Everyday, all the time

week/Frequently

The Nighttime? Would you say...(f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a

MEDICATIONS (Enter responses in table. Do not prompt for each medication in the Medication Code List below.)

The last two questions involve the medicines your child is taking for breathing problems.

27. Since our last contact with you, what medicines has your baby taken, including medicines delivered by a nebulizer or breathing machine at home?	27a. Code	27b. Does he/she take that medicine everyday, sometimes or only when sick? (repeat for each medication)
1		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
2		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
3		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
4		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
5		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
6		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick
7		1 <input type="checkbox"/> Everyday 2 <input type="checkbox"/> Sometimes 3 <input type="checkbox"/> Only when Sick

Medication Code List:

<p>Rescue medicines: 1 Albuterol 2 Proventil 3 Serevent 4 Ventolin 5 Volmax 6 Xopenex</p>	<p>Systemic steroids: 16 Decadron 17 Prednisone 18 Prednisolone</p>
<p>Other Inhaled medications: 7 Cromolyn (Intal) 8 Nedocromil (Tilade)</p>	<p>Leukotriene blocker: 19 Accolate 20 Singulair</p>
<p>Inhaled steroids: 9 Advair 10 Aerobid 11 Azmacort 12 Beclovent 13 Flovent 14 Vanceril 15 Pulmicort</p>	<p>Methylxanthines: 21 Theophylline</p> <p>Diuretic medications: 22 Diuril 23 Lasix 24 Aldactizide 25 Aldactone</p> <p>Miscellaneous / Non-specific 26 Nebulizer 27 Other _____</p>

Since our last contact with you about your child.....

8. How many times has your child stayed in the hospital for one or more nights in a row? |__|__| times

8a. How many of these times were because of wheezing or breathing problems? |__|__| times

9. Since our last contact with you, has your baby's chest sounded wheezy or whistling?

1 Yes 2 No 3 Don't Know *Ask Question 9a for all responses*

9a. "Has your baby's breathing sounded like this?" (play audio clip of wheezing).

1 Yes 2 No 3 Don't Know

9f. Since our last contact with you, during the worst 2 week period, how often has your child's chest sounded wheezy or whistling during:

The Daytime? Would you say... (f.1)

- 1 Never
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The Nighttime? Would you say... (f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a week/Frequently

10. Since our last contact with you, has your child had a cough for more than 3 days when he/she did not have a cold?

1 Yes 2 No *If NO, skip to Question 11*

IF YES TO QUESTION 10

10a. At what time of the day has this cough usually occurred?

(CHECK ALL THAT APPLY)

- 1 In the morning, shortly after rising
- 2 Later in the day
- 3 During the night
- 4 No relation to time of day

10f. Since our last contact with you, during the worst 2-week period, how often has your child had coughing?

The Daytime? Would you say... (f.1)

- 1 Never
- 2 Twice a week or less
- 3 More than two times a week, but not every day
- 4 Everyday, but *not* all the time
- 5 Everyday, all the time

The Nighttime? Would you say... (f.2)

- 1 Never
- 2 Once every two weeks or less
- 3 Once a week
- 4 Two or three times a week
- 5 More than three nights a week/Frequently

MEDICATIONS (Enter responses in table. Do not prompt for each medication in the Medication Code List below.)

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Medication Code List:

<p>Rescue medicines: 1 Albuterol 2 Proventil 3 Serevent 4 Ventolin 5 Volmax 6 Xopenex</p> <p>Other Inhaled medications: 7 Cromolyn (Intal) 8 Nedocromil (Tilade)</p> <p>Inhaled steroids: 9 Advair 10 Aerobid 11 Azmacort 12 Beclovent 13 Flovent 14 Vanceril 15 Pulmicort</p>	<p>Systemic steroids: 16 Decadron 17 Prednisone 18 Prednisolone</p> <p>Leukotriene blocker: 19 Accolate 20 Singulair</p> <p>Methylxanthines: 21 Theophylline</p> <p>Diuretic medications: 22 Diuril 23 Lasix 24 Aldactizide 25 Aldactone</p> <p>Miscellaneous / Non-specific 26 Nebulizer 27 Other _____</p>
--	---

From: Bell, Edward
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo
Subject: RE: CONFIDENTIAL: SUPPORT OXIMETRY PAPER
Date: Friday, February 12, 2010 5:50:37 PM

Also, it looks like you changed the title to make it parallel to Neil's paper (a good idea) but forgot to change the title in the response letter.

Have a good weekend,
Ed

From: Bell, Edward
Sent: Friday, February 12, 2010 4:41 PM
To: Bell, Edward; 'Higgins, Rosemary (NIH/NICHD) [E]'; Wally Carlo
Subject: RE: CONFIDENTIAL: SUPPORT OXIMETRY PAPER

Sorry, the page numbers are OK (at the bottom center). What's the 10 on the second line in the upper right corner of each page?

From: Bell, Edward
Sent: Friday, February 12, 2010 4:39 PM
To: 'Higgins, Rosemary (NIH/NICHD) [E]'; Wally Carlo
Subject: RE: CONFIDENTIAL: SUPPORT OXIMETRY PAPER

I got an error message when I opened the manuscript, and the page numbers are all #10.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Friday, February 12, 2010 4:08 PM
To: dale_phelps@urmc.rochester.edu; 'Finer, Neil'; 'O'Shea, Michael'; 'Duara, Shahnaz'; 'wrich@ucsd.edu'; nxs5@cwru.edu; 'anthony_piazza@oz.ped.emory.edu'; 'Brenda Morris'; 'nirupama_jaroi@urmc.rochester.edu'; 'vivek.narendran@cchmc.org'; 'bsood@med.wayne.edu'; (Luc.Brion@UTSouthwestern.edu); (rohls@unm.edu); aaf2@po.cwru.edu; Abhik Das; alaptook@WIHRI.org; Ambal (ambal@uab.edu); Brad Yoder (Bradley.yoder@hsc.utah.edu); Brenda Poindexter; Carlo Waldemar (E-mail); cotte010@mc.duke.edu; Dennis Wallace; Bell, Edward; Ed Donovan; Ehrenkrantz Richard (E-mail); Ivan Frantz (ifrantz@tuftsmedicalcenter.org); Kennedy, Kathleen A; Kristi Watterberg; Kurt Schibler [kurt.schibler@cchmc.org]; Matthew Bizzarro; Michelle Walsh; Mickey Caplan; Oh William (E-mail); Pablo Sanchez; Poole Kenneth (E-mail); Roger Faix; Ronald GOLDBERG; Seetha Shankaran; Stevenson David (E-mail); Stoll Barbara (E-mail); Tyson Jon (E-mail); VanMeurs, Krisa
Cc: Archer, Stephanie (NIH/NICHD) [E]; 'Cunningham, Meg'; 'Zaterka-Baxter, Kristin'
Subject: CONFIDENTIAL: SUPPORT OXIMETRY PAPER
Importance: High

Hello,
Attached is the resubmission of the CPAP Oximetry paper.

We have allocated time on the upcoming Steering Committee PI call on 2/23 at 3 PM for discussion.

Thanks to everyone for all their effort!!!

The CPAP paper was sent in a separate email.

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: Luc Brion
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: Re: CONFIDENTIAL:CPAP SUPPORT PAPER RESUBMISSION
Date: Friday, February 12, 2010 4:48:56 PM

Rose:
Thanks a lot!
Luc

Luc P. Brion, MD
Professor of Pediatrics
Director, Fellowship Training Program in Neonatal-Perinatal Medicine
The University of Texas Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard, STOP 9063
Dallas, TX 75390-9063
Office: (214) 648-2835
Fax: (214) 648-2481
luc.brion@utsouthwestern.edu

+++++CONFIDENTIALITY NOTICE+++++

All information included in this Communication, including attachments, is strictly confidential and intended solely for use by the addressee(s) identified above, and may contain privileged, confidential, proprietary and/or trade secret information entitled to protection and/or exempt from disclosure under applicable law. If you are not the intended recipient, please take notice that any use, distribution, or copying of this Communication is unauthorized and may be unlawful. If you have received this Communication in error, please notify the sender and delete this Communication from your computer. Please note that any views or opinions presented in this email are solely those of the author and do not necessarily represent those of UT Southwestern. University of Texas Southwestern Medical Center 5323 Harry Hines Blvd., Dallas TX 75390 www.utsouthwestern.edu (<http://www.utsouthwestern.edu/>)

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 2/12/2010 3:47 PM >>>

Hello to all

Attached is the resubmission of the CPAP SUPPORT paper.

We have allocated time on the upcoming Steering Committee PI call on 2/23 at 3 PM for discussion.

Thanks to everyone for all their effort!!!

The Oximetry paper will be sent in a separate email.

Rose
Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

From: [Bell, Edward](#)
To: [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Cc: [Finer, Neil](#); [Wally Carlo](#)
Subject: Secondary proposal for SUPPORT
Date: Friday, February 12, 2010 11:26:48 AM

Rose,
Gil Binenbaum (CHOP) and I are working on the previously discussed proposal to look at the relationship between growth rate and ROP risk in the SUPPORT cohort.
Ed

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mcunningham@rti.org"
Subject: Re: SUPPORT
Date: Friday, February 12, 2010 10:47:18 AM

Nothing - I will send a quick email

From: Cunningham, Meg <mcunningham@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Fri Feb 12 10:46:41 2010
Subject: SUPPORT

Neil didn't send anything did he? Wanted to give James a quick bathroom break if there was nothing to stream.

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Wally Carlo, M.D."; "nfiner@ucsd.edu"
Subject: RE: Disclosure draft for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants
Date: Thursday, February 11, 2010 2:53:00 PM

Let me know if you guys need anything else

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, February 11, 2010 2:53 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Subject: RE: Disclosure draft for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

GREAT!

I have made tracked changes.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thursday, February 11, 2010 1:19 PM
To: Wally Carlo, M.D.; nfiner@ucsd.edu
Subject: RE: Disclosure draft for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Try this

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, February 11, 2010 2:05 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu
Subject: FW: Disclosure draft for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Here is the draft following their style and instructions, We do not have to do it exactly this way but here is a draft.

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: Marcus Humphrey
Sent: Wednesday, February 10, 2010 12:32 AM
To: Wally Carlo, M.D.
Subject: Disclosure draft for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants

Here is my first draft for the disclosure paragraph for The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants, I have not received the disclosure forms from the other authors so there are a lot of blanks on this draft. The second section is just a template that has to be repeated for each author based off of their disclosure form. I have a list of authors but I don't know what they did for the paper if you can help filling in those blanks and who should I contact to get the other authors disclosure forms or do we need to contact each one individually?

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Thursday, February 11, 2010 2:26 PM
To: babel@nejm.org
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: New England Journal of Medicine 09-11783

Hello Brendan

The consent paper is about the number of women approached relative to the number who consented, and compares approached versus non-approached women. This manuscript does not contain any results.

Thanks you

Neil Finer

-----Original Message-----

From: onbehalfof+babel+nejm.org@manuscriptcentral.com
[mailto:onbehalfof+babel+nejm.org@manuscriptcentral.com] On Behalf Of babel@nejm.org
Sent: Thursday, February 11, 2010 11:12 AM
To: Finer, Neil
Subject: New England Journal of Medicine 09-11783

Re: 09-11783 - Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial

Dear Dr. Finer:

I spoke with Caren Solomon regarding your inquiry. As long as the manuscript is only about the consent process and has no overlap with results reported in your NEJM submission, then you are ok not to provide the manuscript. If there is any potential overlap, it is routine that authors send us a copy of the manuscript so we can confirm no substantive overlap. Of course, we can assure you that we will keep this confidential.

Sincerely,

Brendan Abel
Editorial Assistant
New England Journal of Medicine
(617) 487-6584

From: Zaterka-Baxter, Kristin
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support subcom
Date: Wednesday, February 10, 2010 5:11:51 PM

Ok – sorry I missed that
Thanks,
Kris

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, February 10, 2010 5:11 PM
To: Zaterka-Baxter, Kristin
Subject: Re: Support subcom

Closed
I had sent an email to this effect

From: Zaterka-Baxter, Kristin <kzaterka@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Wed Feb 10 17:09:36 2010
Subject: Support subcom

Is the Support subcom open to all or closed to the subcommittee only?
Thanks,
Kris

*Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
P.O. Box 12194
RTP, NC 27709-2194 USA
(tel) 919-485-7750
(fax) 919.485.7762
kzaterka@rti.org
www.rti.org*

*Federal Express/UPS/DHL Shipping Address:
Kris Zaterka-Baxter
RTI International
3040 Cornwallis Road
RTP, NC 27709 USA*

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "nfiner@ucsd.edu"; "wcarlo@peds.uab.edu"
Cc: "wrich@ucsd.edu"; "mgantz@rti.org"; "adas@rti.org"
Subject: Re: Remainder of CPAP reviewer Q&A
Date: Wednesday, February 10, 2010 1:43:48 PM

This is a good plan. The word limit should not apply to this

----- Original Message -----

From: Finer, Neil <nfiner@ucsd.edu>
To: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
Cc: Rich, Wade <wrich@ucsd.edu>; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie <mgantz@rti.org>; Das, Abhik <adas@rti.org>
Sent: Wed Feb 10 13:16:29 2010
Subject: RE: Remainder of CPAP reviewer Q&A

Hi Wally
The manuscript is already over the word limit.
Can we put it at the top of the Acknowledgements??
Neil

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Wednesday, February 10, 2010 9:55 AM
To: Finer, Neil
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Subject: RE: Remainder of CPAP reviewer Q&A

Neil:

But in the papers, we never say what support means. I think we should put it in but we should agree where it should be put in.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Wednesday, February 10, 2010 11:53 AM
To: Wally Carlo, M.D.
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Subject: RE: Remainder of CPAP reviewer Q&A

Hi Wally

SUPPORT was developed on a plane ride after Rose said that we couldn't use the name the ROAST, and then COT and she said to find to a supportive name.

So I used SUPPORT - Surfactant Positive Pressure and Oxygenation Randomized Trial

One other thing - in your letter - the question of how often was sampling done - the answer you gave was correct = 10 seconds. Marie is referring to a secondary done at Case and here with 2 second sampling, but even that data was sampled q 10 seconds for the main analyses.

I hope this helps

Neil

-----Original Message-----

From: Wally Carlo, M.D. [<mailto:WCarlo@peds.uab.edu>]

Sent: Wednesday, February 10, 2010 9:19 AM

To: Finer, Neil

Subject: RE: Remainder of CPAP reviewer Q&A

Neil.

I noticed in my paper I never said what SUPPORT stands for. I could not find it in your paper? Do you have it in? If so, where is it? If not, where should we put it?

wally

Sent from my Windows Mobile phone

-----Original Message-----

From: Finer, Neil <nfiner@ucsd.edu>

Sent: Tuesday, February 09, 2010 1:23 PM

To: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>;

'mgantz@rti.org' <mgantz@rti.org>; 'wcarlo@peds.uab.edu'

<wcarlo@peds.uab.edu>; 'adas@rti.org' <adas@rti.org>

Cc: Rich, Wade <wrich@ucsd.edu>

Subject: RE: Remainder of CPAP reviewer Q&A

OK with me

Thanks

Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]

Sent: Tuesday, February 09, 2010 10:50 AM

To: Finer, Neil; 'mgantz@rti.org'; 'wcarlo@peds.uab.edu'; 'adas@rti.org'

Cc: Rich, Wade

Subject: Re: Remainder of CPAP reviewer Q&A

Neil - can we send to the SUPPORT subcommittee?

Thanks

Rose

From: Finer, Neil <nfiner@ucsd.edu>

To: Gantz, Marie <mgantz@rti.org>; Wally Carlo, M.D.

<WCarlo@peds.uab.edu>; Das, Abhik <adas@rti.org>; Higgins, Rosemary

(NIH/NICHD) [E]

Cc: Rich, Wade <wrich@ucsd.edu>

Sent: Tue Feb 09 13:02:05 2010

Subject: RE: Remainder of CPAP reviewer Q&A

Hello Everyone

Here are the following - a revised manuscript, a letter to the editor which I think is complete and I hope is OK, and the final figures and Tables

Please review. If OK then do whatever is next regarding NRBN approval. When this is done I can upload. Wally and I should upload at similar times.

I look forward to your responses.

Wally, I was in briefly to give my talk - Then I had to get back - Sorry

I missed you

Neil

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Wednesday, February 10, 2010 1:16 PM
To: Wally Carlo, M.D.
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Subject: RE: Remainder of CPAP reviewer Q&A

Hi Wally
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Can we put it at the top of the Acknowledgements??
Neil

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Wednesday, February 10, 2010 9:55 AM
To: Finer, Neil
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Subject: RE: Remainder of CPAP reviewer Q&A

Neil:

But in the papers, we never say what support means. I think we should put it in but we should agree where it should be put in.

Wally

Wally Carlo, M.D.
Edwin M. Dixon Professor of Pediatrics
University of Alabama at Birmingham
Director, Division of Neonatology
Director, Newborn Nurseries
619 South 20th Street
525 New Hillman Building
Birmingham, AL 35233-7335
Phone: 205 934 4680
FAX: 205 934 3100
Cell: 205 266 4004

-----Original Message-----

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Wednesday, February 10, 2010 11:53 AM
To: Wally Carlo, M.D.
Cc: Rich, Wade; Higgins, Rosemary (NIH/NICHD) [E]; Gantz, Marie; Das, Abhik
Subject: RE: Remainder of CPAP reviewer Q&A

Hi Wally
SUPPORT was developed on a plane ride after Rose said that we couldn't use the name the ROAST, and then COT and she said to find to a supportive name.

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I hope this helps

Neil

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]

Sent: Wednesday, February 10, 2010 9:19 AM

To: Finer, Neil

Subject: RE: Remainder of CPAP reviewer Q&A

Neil.

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wally

Sent from my Windows Mobile phone

-----Original Message-----

From: Finer, Neil <nfiner@ucsd.edu>

Sent: Tuesday, February 09, 2010 1:23 PM

To: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>; 'mgantz@rti.org' <mgantz@rti.org>; 'wcarlo@peds.uab.edu'

<wcarlo@peds.uab.edu>; 'adas@rti.org' <adas@rti.org>

Cc: Rich, Wade <wrich@ucsd.edu>

Subject: RE: Remainder of CPAP reviewer Q&A

OK with me

Thanks

Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]

Sent: Tuesday, February 09, 2010 10:50 AM

To: Finer, Neil; 'mgantz@rti.org'; 'wcarlo@peds.uab.edu'; 'adas@rti.org'

Cc: Rich, Wade

Subject: Re: Remainder of CPAP reviewer Q&A

Neil - can we send to the SUPPORT subcommittee?

Thanks

Rose

From: Finer, Neil <nfiner@ucsd.edu>

To: Gantz, Marie <mgantz@rti.org>; Wally Carlo, M.D.

<WCarlo@peds.uab.edu>; Das, Abhik <adas@rti.org>; Higgins, Rosemary (NIH/NICHD) [E]

Cc: Rich, Wade <wrich@ucsd.edu>

Sent: Tue Feb 09 13:02:05 2010

Subject: RE: Remainder of CPAP reviewer Q&A Hello Everyone Here are the following - a revised manuscript, a letter to the editor which I think is complete and I hope is OK, and the final figures and Tables Please review. If OK then do whatever is next regarding NRBN approval.

When this is done I can upload. Wally and I should upload at similar times.

Il look forward to your responses.

Wally, I was in briefly to give my talk - Then I had to get back - Sorry I missed you Neil

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wcarlo@peds.uab.edu"
Subject: Re: Support response
Date: Tuesday, February 09, 2010 5:57:41 PM

Stephanie has them. We usually do this. I am hoping to make it to the office before the end of the week and can look through them.

Thanks
Rose

----- Original Message -----

From: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tue Feb 09 12:06:59 2010
Subject: RE: Support response

Rose.

NEJM requires a paragraph of disclosure summarizing the forms. Have you received the forms from everyone and can I have a copy to prepare the paragraph? I had volunteered to draft the paragraph for each paper (they may differ).

wally

Sent from my Windows Mobile phone

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Tuesday, February 09, 2010 5:30 AM
To: 'nfiner@ucsd.edu' <nfiner@ucsd.edu>; 'wcarlo@peds.uab.edu' <wcarlo@peds.uab.edu>
Cc: 'mcunningham@rti.org' <mcunningham@rti.org>
Subject: Support response

Neil and wally -

Once you have the close to final draft responses for nejm, send them to us for distribution to the subcommittee.

Thanks for all the effort!
Rose

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Tuesday, February 09, 2010 5:34 PM
To: Gantz, Marie
Cc: Higgins, Rosemary (NIH/NICHD) [E]; Das, Abhik; Rich, Wade
Subject: RE:Consent Paper
Attachments: Antenatal consent Response LetterFeb 1 Revision.docx

Hi Marie

We have made the changes to the Antenatal Consent paper suggested by the reviewers, answered the queries we could, and marked some items for your review.

Do you have time to get to this so that the paper can go back to the journal for publication in Pediatrics?

Many thanks

Neil

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Tuesday, February 09, 2010 2:27 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; 'mgantz@rti.org'; 'wcarlo@peds.uab.edu'; 'adas@rti.org'
Cc: Rich, Wade
Subject: RE: Remainder of CPAP reviewer Q&A

OK with me
Thanks
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, February 09, 2010 10:50 AM
To: Finer, Neil; 'mgantz@rti.org'; 'wcarlo@peds.uab.edu'; 'adas@rti.org'
Cc: Rich, Wade
Subject: Re: Remainder of CPAP reviewer Q&A

Neil - can we send to the SUPPORT subcommittee?
Thanks
Rose

From: Finer, Neil <nfiner@ucsd.edu>
To: Gantz, Marie <mgantz@rti.org>; Wally Carlo, M.D. <WCarlo@peds.uab.edu>; Das, Abhik <adas@rti.org>; Higgins, Rosemary (NIH/NICHD) [E]
Cc: Rich, Wade <wrich@ucsd.edu>
Sent: Tue Feb 09 13:02:05 2010
Subject: RE: Remainder of CPAP reviewer Q&A

Hello Everyone

Here are the following – a revised manuscript, a letter to the editor which I think is complete and I hope is OK, and the final figures and Tables

Please review. If OK then do whatever is next regarding NRBN approval. When this is done I can upload. Wally and I should upload at similar times.

Il look forward to your responses.

Wally, I was in briefly to give my talk - Then I had to get back – Sorry I missed you

Neil

From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: "[Rhiannon Ross](#)"
Cc: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#); [Bock, Robert \(NIH/NICHD\) \[E\]](#); [McDonough, Sally \(NIH/NHLBI\) \[E\]](#); [Striar, Diane \(NIH/NHLBI\) \[E\]](#); [Dambrauskas, Susan \(NIH/NIDCD\) \[E\]](#)
Subject: RE: Attachment: ATS 2009 Preview edition
Date: Tuesday, February 09, 2010 9:45:38 AM

Dear Rhiannon,

The federal government has been closed, so I didn't get final word from our media offices about this quote from me and Dr. Higgins (co-chair of the session), (in the "cc" line above), but the following should work fine:

During the noon session "OUTCOMES FROM THE NHLBI-NICHD SUPPORT TRIAL: THE (SURFACTANT POSITIVE AIRWAY PRESSURE AND PULSE OXIMETRY) TRIAL IN EXTREMELY LOW BIRTH WEIGHT (ELBW) INFANTS", results will be presented by the investigators.

*Quote from Carol Blaisdell, M.D. (NHLBI) and Rosemary Higgins M.D. (NICHD):
"This is the largest study to date to assess early ventilation strategies and oximetry targets in extremely preterm infants on outcomes of survival without bronchopulmonary dysplasia. Over 1300 infants were enrolled through the Eunice Kennedy Shriver NICHD Neonatal Research Network, with co-funding from NHLBI. This study is likely to impact care of the most immature preterm infants."*

Carol

Carol J. Blaisdell, M.D.
Medical Officer
Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

From: [Rhiannon Ross \[mailto:rross@ascendmedia.com\]](mailto:rross@ascendmedia.com)
Sent: Friday, February 05, 2010 11:09 AM
To: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
Subject: Re: Attachment: ATS 2009 Preview edition

Thank you, Dr. Blaisdell. If possible, I will need it by end-of-day Monday. LMK if this is not possible.

Rhiannon

On 2/5/10 7:58 AM, "Blaisdell, Carol (NIH/NHLBI) [E]" <blaisdellcj@nhlbi.nih.gov> wrote:

We will send you send something soon--cb

Carol J. Blaisdell, M.D.
Medical Officer

Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

From: Rhiannon Ross [mailto:rross@ascendmedia.com]
Sent: Wednesday, February 03, 2010 4:32 PM
To: Blaisdell, Carol (NIH/NHLBI) [E]
Subject: Attachment: ATS 2009 Preview edition

My apologies. I neglected to attach a copy of the 2009 Preview edition of the *ATS Daily Bulletin*.

----- Forwarded Message

From: Rhiannon Ross <rross@ascendmedia.com>
Date: Wed, 03 Feb 2010 15:25:19 -0600
To: <blaisdellcj@nhlbi.nih.gov>
Conversation: ATS Preview Edition: Interview Request
Subject: RE: ATS Preview Edition: Interview Request

Hello Dr. Blaisdell,

My company will once again produce the *ATS Daily Bulletin*, the newspaper that is distributed prior to and during the annual American Thoracic Society International Conference. Working with ATS communications staff Suzy Logan and Brian Kell, I am writing an overview about the 21 clinical trials/research initiatives that will be presented this year for the Preview edition of this publication. I am highlighting four of these sessions in the article and would like to include your session: **L4: "Outcomes from the NHLBI-NICHD Support Trial: The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Weight (ELBW) Infants."**

If you are agreeable, I would like to obtain a quote or two from you about this trial to include in the article. I am attaching a copy of the article on clinical trials/research initiatives that ran in last year's Preview edition to give you an idea of what I'm looking for in terms of a quote (See: "Conference Features Sessions on Research Efforts, Clinical Trials," bottom of page 1, continuing on page 9). I will structure the 2010 article on this 2009 article.

You may e-mail me your quote, or if you prefer, I can call you. I should only need about five or 10 minutes of your time. Just let me know what time and day work best for you. I am also available this weekend. (Note that I am in the Central Time Zone.) Once I have a draft, I will send it to you for your comments. Then the ATS communications staff will edit and I will send you a final version for approval. The Preview edition will be mailed to ATS members in March.

Thank you for your assistance,

Rhiannon Ross
Medical Editor

Ascend Media
7015 College Blvd., Ste. 600
Overland Park, KS 66210
Office: 913-344-1478
Fax: 913-469-1126
Mobile: 913-596-0581

----- End of Forwarded Message

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "wcarlo@peds.uab.edu"; "nfiner@ucsd.edu"
Cc: "mcunningham@rti.org"
Subject: Re: Support response
Date: Tuesday, February 09, 2010 9:45:19 AM

No problem - we just want it for discussion for Thursday

Thanks -hope your travel itinerary avoids the mid-atlantic region

Rose

----- Original Message -----

From: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu <nfiner@ucsd.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>
Cc: mcunningham@rti.org <mcunningham@rti.org>
Sent: Tue Feb 09 09:43:46 2010
Subject: RE: Support response

Rose.

I will get it to you tomorrow. I am in California traveling all day.

Neil.

I missed you yesterday.

wally

Sent from my Windows Mobile phone

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Tuesday, February 09, 2010 5:30 AM
To: 'nfiner@ucsd.edu' <nfiner@ucsd.edu>; 'wcarlo@peds.uab.edu' <wcarlo@peds.uab.edu>
Cc: 'mcunningham@rti.org' <mcunningham@rti.org>
Subject: Support response

Neil and wally -

Once you have the close to final draft responses for nejm, send them to us for distribution to the subcommittee.

Thanks for all the effort!

Rose

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; julie-lindower@uiowa.edu; CBackstrom@salud.unm.edu; mball@leland.stanford.edu; rbara@med.wayne.edu; mcollins@peds.uab.edu; scosby@peds.uab.edu; sandra.grimes@duke.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; ahensman@wihri.org; karen-johnson@uiowa.edu; monica.konstantino@yale.edu; bmackinnon@tuftsmedicalcenter.org; Georgia.E.McDavid@uth.tmc.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; karen.osborne@hsc.utah.edu; ldw@iupui.edu; NAmbalavanan@peds.uab.edu; dpcarit@emory.edu; cotte010@mc.duke.edu; WOH@Lifespan.org; rohls@salud.unm.edu; dstevenson@stanford.edu; Jon.E.Tyson@uth.tmc.edu; bsood@med.wayne.edu; Bradley.yoder@hsc.utah.edu; Zhang, Jun (NIH/NICHD) [E]; edward-bell@uiowa.edu; wcarlo@peds.uab.edu; Cbackstrom@salud.unm.edu; mball@leland.stanford.edu; rbara@med.wayne.edu; mcollins@peds.uab.edu; scosby@peds.uab.edu; sandra.grimes@duke.edu; grisbyca@ucmail.uc.edu; ellen_hale@oz.ped.emory.edu; ahensman@wihri.org; karen-johnson@uiowa.edu; monica.konstantino@yale.edu; BMackinnon@tuftsmedicalcenter.org; Georgia.E.McDavid@uth.tmc.edu; Nancy.Miller@UTSouthwestern.edu; nxs5@cwru.edu; Karen.Osborne@hsc.utah.edu; ldw@iupui.edu; NAmbalavanan@peds.uab.edu; dpcarit@emory.edu; cotte010@mc.duke.edu; WOH@Lifespan.org; rohls@salud.unm.edu; dstevenson@stanford.edu; jon.e.tyson@uth.tmc.edu; bsood@med.wayne.edu; bradley.yoder@hsc.utah.edu; Zhang, Jun (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]; edward-bell@uiowa.edu; wcarlo@peds.uab.edu; richard.ehrenkranz@yale.edu; Roger.Faix@hsc.utah.edu; ifrantz@tuftsmedicalcenter.org; goldb008@mc.duke.edu; Higgins, Rosemary (NIH/NICHD) [E]; Kathleen.A.Kennedy@uth.tmc.edu; alaptok@WIHRI.org; bpoindex@iupui.edu; Pablo.Sanchez@UTSouthwestern.edu; kurt.schibler@cchmc.org; sshankar@med.wayne.edu; [SCRNI] Stoll, Barbara; vanmeurs@leland.stanford.edu; mcw3@cwru.edu; kwatterberg@salud.unm.edu; mcaplan@northshore.org; Luc.Brion@utsouthwestern.edu; Cunningham, Meg; Zaterka-Baxter, Kristin; Das, Abhik; Pickett, James; Gantz, Marie; Auman, Jeanette O.; Poole, W. Kenneth; Huitema, Carolyn Petrie; Nolen, Tracy; Wallace, Dennis; bbatton@siu.med.edu; BENJA005@dcri.duke.edu; alexis.davis@stanford.edu; dale_phelps@urmc.rochester.edu; mblakely@utm.edu; eferandez@salud.unm.edu; srhinz@stanford.edu; tarah-colaizy@uiowa.edu; julie-lindower@uiowa.edu; schelonk@ohsu.edu; debra.camputaro@yale.edu; jwaidne@emory.edu; gonza025@mc.duke.edu; axt25@po.cwru.edu; Karen.Kirby@UTSouthwestern.edu; lmoore@med.wayne.edu; Nancy.M.Smith@uth.tmc.edu; msumner@peds.uab.edu; bvecchio@careNE.org; janiwall@iupui.edu; twrencox@uthsc.edu; jonathan-klein@uiowa.edu; gsokol@iupui.edu; kimberly.fisher@duke.edu; stephanie.crosby@duke.edu; Kendrick, Douglas F. (in StatEpi); clclark@med.unc.edu; dhwilson@iupui.edu; Matt Laughon@med.unc.edu; bvohr@wihri.org
Cc: Zaterka-Baxter, Kristin; Das, Abhik; Pickett, James; Gantz, Marie; Auman, Jeanette O.; Poole, W. Kenneth; Huitema, Carolyn Petrie; Nolen, Tracy; Wallace, Dennis; debra.camputaro@yale.edu; jwaidne@emory.edu; gonza025@mc.duke.edu; axt25@po.cwru.edu; Karen.Kirby@UTSouthwestern.edu; lmoore@med.wayne.edu; Nancy.M.Smith@uth.tmc.edu; msumner@peds.uab.edu; bvecchio@careNE.org; janiwall@iupui.edu; twrencox@uthsc.edu; vwilli4@emory.edu; Rogers, Christine (NIH/NICHD) [E]; Johnson, Nichole (NIH/OD) [E]; Spong, Catherine (NIH/NICHD) [E]
Subject: RE: ++++++urgent Steering committee meeting update++++++
Date: Monday, February 08, 2010 11:05:59 AM

I apologize if you are receiving this email a second time, but it does not appear that all were copied on the original email.

Also, please note that all sleeping room at the Bolger have been cancelled.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Monday, February 08, 2010 10:03 AM
To: Archer, Stephanie (NIH/NICHD) [E]; Cunningham, Meg; 'julie-lindower@uiowa.edu'; 'CBackstrom@salud.unm.edu'; 'mball@leland.stanford.edu'; 'rbara@med.wayne.edu'; 'mcollins@peds.uab.edu'; 'scosby@peds.uab.edu'; 'sandra.grimes@duke.edu'; 'grisbyca@email.uc.edu'; 'ellen_hale@oz.ped.emory.edu'; 'ahensman@wihri.org'; 'karen-johnson@uiowa.edu'; 'monica.konstantino@yale.edu'; 'bmackinnon@tuftsmedicalcenter.org'; 'Georgia.E.McDavid@uth.tmc.edu'; 'Nancy.Miller@UTSouthwestern.edu'; 'nxs5@cwru.edu'; 'karen.osborne@hsc.utah.edu'; 'ldw@iupui.edu'; 'NAmbalavanan@peds.uab.edu'; 'dpcarit@emory.edu'; 'cotte010@mc.duke.edu'; 'WOH@Lifespan.org'; 'rohls@salud.unm.edu'; 'dstevenson@stanford.edu'; 'Jon.E.Tyson@uth.tmc.edu'; 'bsood@med.wayne.edu'; 'Bradley.yoder@hsc.utah.edu'; Zhang, Jun (NIH/NICHD) [E]; 'edward-bell@uiowa.edu'; 'wcarlo@peds.uab.edu'
Cc: Zaterka-Baxter, Kristin; Das, Abhik; Pickett, James; Gantz, Marie; Auman, Jeanette O.; Poole, W. Kenneth; Huitema, Carolyn Petrie; Nolen, Tracy; Wallace, Dennis; 'debra.camputaro@yale.edu'; 'jwaidne@emory.edu'; 'gonza025@mc.duke.edu'; 'axt25@po.cwru.edu'; 'Karen.Kirby@UTSouthwestern.edu'; 'lmoore@med.wayne.edu'; 'Nancy.M.Smith@uth.tmc.edu'; 'msumner@peds.uab.edu'; 'bvecchio@careNE.org'; 'janiwall@iupui.edu'; 'twrencox@uthsc.edu'; 'vwilli4@emory.edu'; Rogers, Christine (NIH/OD) [E]; Johnson, Nichole (NIH/OD) [E]; Spong, Catherine

(NIH/NICHD) [E]

Subject: ++++++urgent Steering committee meeting update+++++

Due to the inclement weather in Washington and the forecast of another storm for Tuesday-Wednesday (5-10 more inches of snow), we will hold the meeting by teleconference so folks will not need to travel to DC (airports are still closed, no above ground metro).

We are in the process of revising the agenda. Subcommittee meetings that can be arranged by separate teleconference will be set up. The SUPPORT Subcommittee and Optimizing Cooling will meet. The remainder likely may be done at another time, unless there are urgent issues. We did meet by phone in 2003 when Hurricane Isabel came through.

Let me know if there are questions. All handouts/presentations will be posted (either on the RTI website or via a web meeting site which may be set up).

Rose

From: Archer, Stephanie (NIH/NICHD) [E]

To: Higgins, Rosemary (NIH/NICHD) [E]; 'Cunningham, Meg' <mcunningham@rti.org>; julie-lindower@uiowa.edu <julie-lindower@uiowa.edu>; Cbackstrom@salud.unm.edu <Cbackstrom@salud.unm.edu>; mball@leland.stanford.edu <mball@leland.stanford.edu>; rbara@med.wayne.edu <rbara@med.wayne.edu>; mcollins@peds.uab.edu <mcollins@peds.uab.edu>; scosby@peds.uab.edu <scosby@peds.uab.edu>; sandra.grimes@duke.edu <sandra.grimes@duke.edu>; grisbyca@email.uc.edu <grisbyca@email.uc.edu>; ellen_hale@oz.ped.emory.edu <ellen_hale@oz.ped.emory.edu>; ahensman@wihri.org <ahensman@wihri.org>; karen-johnson@uiowa.edu <karen-johnson@uiowa.edu>; monica.konstantino@yale.edu <monica.konstantino@yale.edu>; BMackinnon@tuftsmedicalcenter.org <BMackinnon@tuftsmedicalcenter.org>; Georgia.E.McDavid@uth.tmc.edu <Georgia.E.McDavid@uth.tmc.edu>; Nancy.Miller@UTSouthwestern.edu <Nancy.Miller@UTSouthwestern.edu>; nxs5@cwru.edu <nxs5@cwru.edu>; Karen.Osborne@hsc.utah.edu <Karen.Osborne@hsc.utah.edu>; ldw@iupui.edu <ldw@iupui.edu>; NAmbalavanan@peds.uab.edu <NAmbalavanan@peds.uab.edu>; dpcarl@emory.edu <dpcarl@emory.edu>; cotte010@mc.duke.edu <cotte010@mc.duke.edu>; WOh@Lifespan.org <WOh@Lifespan.org>; rohls@salud.unm.edu <rohls@salud.unm.edu>; dstevenson@stanford.edu <dstevenson@stanford.edu>; jon.e.tyson@uth.tmc.edu <jon.e.tyson@uth.tmc.edu>; bsood@med.wayne.edu <bsood@med.wayne.edu>; bradley.yoder@hsc.utah.edu <bradley.yoder@hsc.utah.edu>; Zhang, Jun (NIH/NICHD) [E]; edward-bell@uiowa.edu <edward-bell@uiowa.edu>; wcarlo@peds.uab.edu <wcarlo@peds.uab.edu>; richard.ehrenkranz@yale.edu <richard.ehrenkranz@yale.edu>; Roger.Faix@hsc.utah.edu <Roger.Faix@hsc.utah.edu>; ifrantz@tuftsmedicalcenter.org <ifrantz@tuftsmedicalcenter.org>; goldb008@mc.duke.edu <goldb008@mc.duke.edu>; Kathleen.A.Kennedy@uth.tmc.edu <Kathleen.A.Kennedy@uth.tmc.edu>; alaptook@WIHRI.org <alaptook@WIHRI.org>; bpoindex@iupui.edu <bpoindex@iupui.edu>; Pablo.Sanchez@UTSouthwestern.edu <Pablo.Sanchez@UTSouthwestern.edu>; kurt.schibler@cchmc.org <kurt.schibler@cchmc.org>; sshankar@med.wayne.edu <sshankar@med.wayne.edu>; [SCRN] Stoll, Barbara <barbara_stoll@oz.ped.emory.edu>; vanmeurs@leland.stanford.edu <vanmeurs@leland.stanford.edu>; mcw3@cwru.edu <mcw3@cwru.edu>; kwatterberg@salud.unm.edu <kwatterberg@salud.unm.edu>; mcaplan@northshore.org <mcaplan@northshore.org>; Luc.Brion@utsouthwestern.edu <Luc.Brion@utsouthwestern.edu>; bbatton@siumed.edu <bbatton@siumed.edu>; BENJA005@dcri.duke.edu <BENJA005@dcri.duke.edu>; alexis.davis@stanford.edu <alexis.davis@stanford.edu>; dale_phelps@urmc.rochester.edu <dale_phelps@urmc.rochester.edu>; mblakely@utm.edu <mblakely@utm.edu>; efernandez@salud.unm.edu <efernandez@salud.unm.edu>; srhintz@stanford.edu <srhintz@stanford.edu>; tarah-colaizy@uiowa.edu <tarah-colaizy@uiowa.edu>; julie-lindower@uiowa.edu <julie-lindower@uiowa.edu>; schelonk@ohsu.edu <schelonk@ohsu.edu>; gsokol@iupui.edu <gsokol@iupui.edu>

Cc: Zaterka-Baxter, Kristin <kzaterka@rti.org>; Das, Abhik <adas@rti.org>; Pickett, James <japickett@rti.org>; Gantz, Marie <mgantz@rti.org>; Auman, Jeanette O. <joa@rti.org>; Poole, W. Kenneth <poo@rti.org>; Huitema, Carolyn Petrie <petrie@rti.org>; Nolen, Tracy <tnolen@rti.org>; Wallace, Dennis <dwallace@rti.org>; debra.camputaro@yale.edu <debra.camputaro@yale.edu>;

jwaidne@emory.edu <jwaidne@emory.edu>; gonza025@mc.duke.edu <gonza025@mc.duke.edu>;
axt25@po.cwru.edu <axt25@po.cwru.edu>; Karen.Kirby@UTSouthwestern.edu
<Karen.Kirby@UTSouthwestern.edu>; lmoore@med.wayne.edu <lmoore@med.wayne.edu>;
Nancy.M.Smith@uth.tmc.edu <Nancy.M.Smith@uth.tmc.edu>; msumner@peds.uab.edu
<msumner@peds.uab.edu>; bvecchio@careNE.org <bvecchio@careNE.org>; janiwall@iupui.edu
<janiwall@iupui.edu>; twrencox@uthsc.edu <twrencox@uthsc.edu>; vwilli4@emory.edu
<vwilli4@emory.edu>; Rogers, Christine (NIH/OD) [E]; Johnson, Nichole (NIH/OD) [E]

Sent: Thu Feb 04 10:00:05 2010

Subject: NRN Steering Committee Meeting | PHOTOCOPY REQUESTS DUE TOMORROW

Just a reminder to please send us any materials you need photocopied by TOMORROW, Friday,
February 5th.

Stephanie Wilson Archer
The Eunice Kennedy Shriver
National Institute of Child Health and Human Development
Pregnancy & Perinatology Branch
6100 Executive Boulevard, Room 4B03
Rockville, MD 20852

Tel. 301-496-0430

Fax 301-496-3790

archerst@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]

Sent: Friday, January 29, 2010 4:37 PM

To: 'Cunningham, Meg'; julie-lindower@uiowa.edu; Cbackstrom@salud.unm.edu;
mbball@leland.stanford.edu; rbara@med.wayne.edu; mcollins@peds.uab.edu; scosby@peds.uab.edu;
sandra.grimes@duke.edu; grisbyca@email.uc.edu; ellen_hale@oz.ped.emory.edu; ahensman@wihri.org;
karen-johnson@uiowa.edu; monica.konstantino@yale.edu; BMackinnon@tuftsmedicalcenter.org;
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Karen.Osborne@hsc.utah.edu; ldw@iupui.edu; NAMBALAVANAN@peds.uab.edu; dpcarl@emory.edu;
cotte010@mc.duke.edu; WOh@Lifespan.org; rohls@salud.unm.edu; dstevenson@stanford.edu;
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Cc: Zaterka-Baxter, Kristin; Das, Abhik; Pickett, James; Gantz, Marie; Auman, Jeanette O.; Poole, W.
Kenneth; Huitema, Carolyn Petrie; Nolen, Tracy; Wallace, Dennis; debra.camputaro@yale.edu;
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Subject: RE: February SC Meeting Concepts

For the upcoming steering committee meeting, please email materials by Friday February 5. If you do not have materials available at this time, please email your information to the appropriate subcommittee or steering committee.

In addition, the NICHD Pregnancy and Perinatology Offices will undergo a renovation

and will be **inaccessible from February 18-22**. If there are vital items that you will need during this time from the NICHD staff, please plan accordingly as we may not be able to access all files.

Dress code for the meeting – casual – it has been a very cold winter in the DC area.

Rose

From: Cunningham, Meg
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: agenda
Date: Friday, February 05, 2010 12:18:57 PM

Was I supposed to add a SUPPORT meeting on day 1? I didn't, but feel like I should have. Overlapping with NEC?

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From: Blaisdell, Carol (NIH/NHLBI) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: FW: Attachment: ATS 2009 Preview edition
Date: Thursday, February 04, 2010 12:17:37 PM
Attachments: [ATS_Preview.pdf](#)

Dear Rose,

The ATS is interested in a brief "quote" to use for the newsletter about SUPPORT.

See attached for the way this newsletter highlights clinical studies presentations at ATS 2009.

I would be happy to coordinate with you a quote, or if you prefer I can do it with our press office at NHLBI.

I am at review this AM, but around a bit this afternoon or tomorrow most of the day if you want to discuss.

Carol
(301) 435-0222 phone

From: Rhiannon Ross [mailto:rross@ascendmedia.com]
Sent: Wednesday, February 03, 2010 4:32 PM
To: Blaisdell, Carol (NIH/NHLBI) [E]
Subject: Attachment: ATS 2009 Preview edition

My apologies. I neglected to attach a copy of the 2009 Preview edition of the *ATS Daily Bulletin*.

----- Forwarded Message

From: Rhiannon Ross <rross@ascendmedia.com>
Date: Wed, 03 Feb 2010 15:25:19 -0600
To: <blaisdellcj@nhlbi.nih.gov>
Conversation: ATS Preview Edition: Interview Request
Subject: RE: ATS Preview Edition: Interview Request

Hello Dr. Blaisdell,

My company will once again produce the *ATS Daily Bulletin*, the newspaper that is distributed prior to and during the annual American Thoracic Society International Conference. Working with ATS communications staff Suzy Logan and Brian Kell, I am writing an overview about the 21 clinical trials/research initiatives that will be presented this year for the Preview edition of this publication. I am highlighting four of these sessions in the article and would like to include your session: **L4: "Outcomes from the NHLBI-NICHD Support Trial: The Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Weight (ELBW) Infants."**

If you are agreeable, I would like to obtain a quote or two from you about this trial to include in the article. I am attaching a copy of the article on clinical trials/research initiatives that ran in last year's Preview edition to give you an idea of what I'm looking for in terms of a quote (See: "Conference Features Sessions on Research Efforts, Clinical Trials," bottom of page 1,

continuing on page 9). I will structure the 2010 article on this 2009 article.

You may e-mail me your quote, or if you prefer, I can call you. I should only need about five or 10 minutes of your time. Just let me know what time and day work best for you. I am also available this weekend. (Note that I am in the Central Time Zone.) Once I have a draft, I will send it to you for your comments. Then the ATS communications staff will edit and I will send you a final version for approval. The Preview edition will be mailed to ATS members in March.

Thank you for your assistance,

Rhiannon Ross
Medical Editor
Ascend Media
7015 College Blvd., Ste. 600
Overland Park, KS 66210
Office: 913-344-1478
Fax: 913-469-1126
Mobile: 913-596-0581

----- End of Forwarded Message



ATS DAILY BULLETIN

SAN DIEGO • MAY 15-20, 2009 • PREVIEW EDITION

P3 SLEEP, MV POSTGRAD COURSES

P5 2009 PAR SYMPOSIUM

P6 KEY ASSEMBLY ABSTRACTS

MEETING HIGHLIGHT

ATS 2009 in San Diego Offers Best in Pulmonary, Critical Care, Sleep Science

The American Thoracic Society's 2009 International Conference is shaping up to be one of the most exciting conferences for the ATS, making attendance at this outstanding educational venue well-worth the effort of pulmonary, critical care and sleep scientists and clinicians. Because of the 5,395 abstracts received this year, conference planners anticipate great attendance for ATS 2009 in San Diego.

"Generally, West Coast conferences are well-attended. Attendees like San Diego, the nearby attractions are appealing, the weather is usually great and the convention center is nicely designed," said conference committee chair Monica Kraft, M.D. "The main draw, though, is the science and education we offer."

ATS President Jo Rae Wright, Ph.D., concurs. "The conference provides an outstanding blend of basic, clinical and translational science and up-to-date overviews of the state of the art in research and clinical care," Dr. Wright said. "There is a strong interdisciplinary approach in planning the conference to tackle the biggest problems facing patients, their families and the health of the public."

The ATS International Conference Committee always incorporates new elements to keep programming fresh. New this year, Dr. Kraft said, are late-breaking clinical trials; an increased focus on genetics and genomics; more attention to sleep medicine; discus-



Photo courtesy of San Diego CVB

Make plans now to attend the 2009 ATS International Conference May 15-20 in San Diego.

sion of personalized medicine and what that means for patients; programming from the new ATS Assembly on Pulmonary Rehabilitation; and increased emphasis on serving the needs of pulmonary, critical care and sleep medicine trainees.

At the same time, blockbuster mainstays return to the program year after year. These include the ATS Awards Session from 4:30 to 6:30 p.m., on Sunday, May 17, where the

Amberson Lecture is presented; the ATS Public Advisory Roundtable symposium on pulmonary fibrosis from 1:30 to 4 p.m., also on Sunday; and the ATS Membership Meeting, which includes the President's Lecture, from 11:30 a.m. to 1 p.m., on Tuesday, May 19. The ever-popular Clinical Year in Review morning sessions are scheduled Sunday through Wednesday, May 20, while see ATS 2009, page 4

Pre-register Today for ATS 2009 International Conference

Pre-register on or before April 20 to secure the discounted rate to attend the American Thoracic Society's 2009 International Conference in San Diego.

FROM APRIL 21 FORWARD, REGISTRANTS will pay the full conference fee, a full \$50 more than the fee up to April 20.

Conference attendees are strongly encouraged to pre-register by visiting the ATS Web site at www.thoracic.org/go/international-conference. Attendees may also pre-register by phone at (866) 635-3582 or (508) 743-8518, by fax at (508) 759-4552 or by mail at International Conference San Diego 2009, c/o Convention Data Services, 107 Waterhouse Road, Bourne, MA 02532.

Pre-registration is open for ATS 2009 any time prior to the start of the conference on May 15 when the first post-graduate courses begin in San Diego. If you prefer, you can also register onsite at any time during the meeting at the registration counters outside of Hall D on the ground level of the San Diego Convention Center.

Plenty of Fun in the Sun

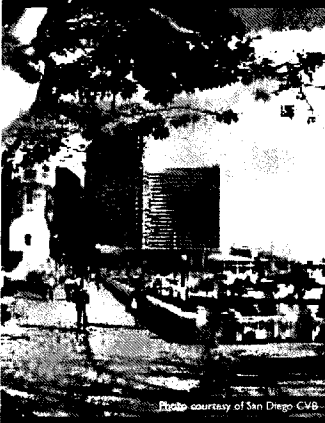


Photo courtesy of San Diego CVB

Adjacent to the San Diego Convention Center, Seaport Village offers many shopping and dining choices and four miles of tree-lined paths.

Conference Features Sessions on Research Efforts, Clinical Trials

Each year, researchers, scientists and clinicians gather at the American Thoracic Society's International Conference to hear about the latest findings of ongoing clinical trials and other research initiatives. ATS 2009 will feature 19 sessions sponsored by organizations like the National Heart, Lung, and Blood Institute (NHLBI), the National Aeronautics and Space Administration (NASA), the U.S. Food and Drug Administration (FDA) and the National Institute of Occupational Safety and Health. These sessions will address everything from the connection between urban environment and childhood asthma to the effect of moon dust on lungs.

At the Recruitment Pavilion in the 2800 row of the Exhibit Hall, attendees interested in breaking research will also have the opportunity to browse the organizations and institutions seeking to recruit



ATS 2009 presents the latest in ongoing clinical trials and research initiatives.

pulmonary, critical care or sleep medicine professionals for involvement in clinical trials or research studies. The Exhibit Hall will be open from May 17 to 19.

Among the 19 clinical trial sessions is

a key one that addresses "Urban Environment and Childhood Asthma (URECA): Insights to Early Markers of Immune Development and Asthma in the Inner City," which will take place from noon to 1 p.m. on Sunday, May 17. Sponsored by the National Institute of Allergy and Infectious Disease (NIAID) and the Inner City Asthma Consortium, the session will be chaired by Peter J. Gergen, M.D., M.P.H., medical officer of NIAID's Division of Allergy, Immunology and Transplantation.

In URECA, "investigators created a birth cohort, now several years in progress, where cytokines were measured in cord blood of infants who were then followed very closely for development of wheezing, allergic disease, food allergies and aeroallergens over the first years of life," Dr. Gergen said. "We want to present early birth cohort

see RESEARCH, page 9



ATS

We help the world breathe
PULMONARY • NUTRITION • ALLERGY

2009 International Conference
San Diego



EVENING
POSTGRADUATE SEMINAR

SESSION E3

COPD: A Systemic Disease?

Douglas Pavilion C/D, Manchester Grand Hyatt Hotel
Sunday 17th May 2009 6:30pm - 9:00pm

Agenda

Chair: Fernando Martinez, MD
Taubman Cancer, Ann Arbor, Michigan, USA

6:30pm - 7:00pm Dinner

7:00pm Pathologic findings in COPD
Leo Fabbri, MD
University of Modena & Reggio Emilia, Italy

7:20pm Clinical significance of inflammation in COPD
Stephen Raywood, MD
University of Nebraska Medical Center, Omaha, Nebraska

7:40pm Systemic manifestations of COPD
Benedetto Celli, MD
St. Elizabeth's Medical Center, Boston, Massachusetts

8:00pm Do current therapies modify systemic effects of COPD?
Klaus Rabe, MD
Leiden University Medical Centre, Leiden, The Netherlands

8:20pm Can or should future therapies target systemic manifestations of disease?
Peter Gierthy, MD
University Hospital Aintree, Liverpool, United Kingdom

8:40pm - 9:00pm Panel Discussion

This event is supported by
an educational grant from





SAN DIEGO FUN FACTS

Photos courtesy of San Diego CVB

A Dozen Fun Facts Prove San Diego as Ideal Destination

The facts are incontrovertible. San Diego is a big draw for the convention, tourist, business, manufacturing and entertainment sectors. These 12 fun facts demonstrate why.



Balboa Park

The sun shines 264 days of the year, and temperatures remain relatively constant year-round. Daytime temperatures range from 70 to 78 degrees in the summer and 63 to 67 degrees in the winter.

San Diego is surrounded by 70 miles of beaches. Other major tourist destinations include Balboa Park, the San Diego Zoo, SeaWorld San Diego, nearby Wild Animal Park and Legoland.

San Diego hosted two World's Fairs (1915 and 1935), the Panama-California Exposition in 1915 and the California Pacific International Exposition in 1935. Many of the Spanish/Baroque-style buildings in Balboa Park were built for these expositions.

The San Diego Zoo is home to 4,000 animals of more than 800 species and is one of few zoos in the world to house pandas.

The Hotel del Coronado on Coronado Island is the largest wooden structure in the United States. Presidents and celebrities have enjoyed lodging at this stately hotel, which is located on one of the best beaches in the U.S.

Since 1898, more than 500 movies and television programs have been filmed in San Diego. The first 1898 Edison Company production featured a short street scene of downtown, complete with a double-decker trolley.

With 2.8 million residents, San Diego is the nation's eighth largest city. Its leading industries are manufacturing, defense, tourism and agriculture. Telecommunications, software and biotech are among the fastest growing sectors.

San Diego owes much of its economy to the Port of San Diego, which manages the maritime operations of San Diego harbor. The port houses the only major submarine and shipbuilding yards on the West Coast, the largest naval fleet in the world and the winter terminal for four major cruise ship lines.

San Diego County produces more than 40 percent of California's avocado crop, which in turn produces 95 percent of the nation's avocados.



According to U.S. Census Bureau education rankings, 40.4 percent of San Diego residents ages 25 and older have bachelor's degrees.

Downtown San Diego has undergone extensive urban renewal since the early 1980s, beginning with the opening of the Horton Plaza shopping mall, the revival of the Gaslamp Quarter and the expansion of the San Diego Convention Center. The 16-block historic Gaslamp Quarter is famous for its turn-of-the-century Victorian architecture and is home to boutiques, art galleries and specialty shops.

San Diego is home of the first European settlement on the West Coast. The first European to visit the region was Portuguese-born explorer Juan Rodrigues Cabrillo, who sailed under the Spanish flag.



Gaslamp Quarter

Postgraduate Courses Present Latest in Sleep Medicine, Mechanical Ventilation

Four PG courses on Friday and Saturday, May 15 and 16, will provide attendees with the latest on sleep disorders and mechanical ventilation.

Sleep Medicine

"The ATS considers sleep medicine one of its three pillars, and our aim is to provide postgraduate courses that reflect this prominence," said Mary J. Morrell, Ph.D., chair of the ATS Assembly on Sleep and Respiratory Neurobiology. "These day-long courses will provide attendees with a review of the latest advances in the field by international experts. The opportunity to interact with this faculty is an added value for attendees."

The sleep postgraduate courses are not normally linked, said course co-chair Ilene M. Rosen, M.D., program director of the Penn Sleep Fellowship at the Hospital of the University of Pennsylvania in Philadelphia. Dr. Rosen co-chairs the sleep postgraduate courses with Susheel P. Patil, M.D., Ph.D., an instructor in pulmonary and critical care medicine, and Brian McGinley, M.D., assistant professor in pediatric pulmonology, both of Johns Hopkins Medicine, in Baltimore.

"By attending both days, you will get a great overview of sleep medicine, which will include in-depth coverage of sleep biology and the non-pulmonary disorders, as well as pulmonary-related disorders, including pediatric elements," Dr. Rosen said. "Pulmonary attendees had given us

feedback that they would like more in-depth coverage of the non-pulmonary sleep topics."

Both days will include a pre-test assessment with session review to identify areas of weakness that require further study, said Dr. Morrell, reader in respiratory physiology at the National Heart and Lung Institute at Imperial College in London. At each day's end, sessions will present summaries of diagnostic and management paradigms using a case-based format with review of sleep-related diagnostic testing.

The first course, PG13, will cover the neurobiology and physiology of normal sleep and will address non-pulmonary disorders, including insomnia, restless leg syndrome and the hypersomnias, Dr. Rosen said.

"This information may be particularly useful to U.S. physicians preparing for the ABIM Sleep Medicine Board Examination as a preliminary review," she said. "A solid knowledge base in both pulmonary and non-pulmonary sleep disorders is required for sleep medicine certification."

The second course, PG 28, will focus on pediatric sleep medicine and sleep-disordered breathing in adults. The pediatric sleep medicine portion will include sleep

studies in children, sleep-disordered breathing in children and a review of neurologic sleep disorders manifested in children, Dr. Rosen added. The remainder of the course will address all sleep apnea diagnosis management and treatment and the interface between pulmonary disorders and sleep disorders.

"There will be something for everyone in these sleep medicine postgraduate courses from thorough reviews of sleep disorders to up-and-coming, push-the-envelope treatments," Dr. Rosen concluded.

Mechanical Ventilation

The postgraduate courses on mechanical ventilation at the ATS International Conferences "have become classic ones," said Stefano Nava, M.D., who chairs two such courses being sponsored this year by the ATS Assembly on Critical Care. For 2009, the assembly developed "twin" postgraduate courses on mechanical ventilation and weaning to serve as a comprehensive "two-day immersion" into these topics.

"The number of mechanically ventilated patients is growing, taking up an increasing number of critical care beds in hospitals," said Dr. Nava, chief of the Respiratory Intensive Care Unit at the Fondazione S.

POSTGRADUATE COURSES

PG6: "Mechanical Ventilation: State of the Art"

PG20: "Weaning from Mechanical Ventilation"

PG 13: "Comprehensive Update in Sleep Medicine. Day 1: Sleep Biology and Non-Pulmonary Sleep" *

PG28: "Comprehensive Update in Sleep Medicine. Day 2: Pediatric Pulmonary Sleep Medicine" *

**These courses can be taken separately, or together. Those who register for both will receive a 10 percent discount on the second course fee.*

Maugeri Istituto Scientifico in Pavia, Italy. "Unfortunately, residents and fellows worldwide are not always ready to manage these patients because mechanical ventilation has not been a deeply explored field."

PG6: "Mechanical Ventilation: State of the Art" begins with a "back-to-the-basics" session, after which international leaders will outline the current state of knowledge, along with perspectives on how to integrate this information into clinical care.

"In addition to fundamentals, the course will be about what's new and what's hot see MECHANICAL VENTILATION, page 10

ATS 2009 Exhibit Hall Offers Enticing New Features

"We encourage all attendees to visit the Exhibit Hall this year. Whether you want more information on a new product or service, are interested in being an investigator in new clinical trials or want to talk with patients about various pulmonary diseases, the ATS 2009 Exhibit Hall has something that can benefit everyone who attends the ATS International Conference."

Michelle Turenne, director of ATS corporate alliances and development

The Exhibit Hall returns to ATS 2009 with practical yet engaging enhancements and mainstay features back by popular demand. The 200-exhibitor event will be open from Sunday, May 17, through Tuesday, May 19, in Halls B1-C of the San Diego Convention Center.

New features in the Exhibit Hall this year include Product Theatres complete with complimentary box lunches; a Discovery Zone highlighting smaller exhibitors with some of the latest technology available in pulmonary, critical care and sleep medicine; and the Recruitment Pavilion, where members and attendees can talk with companies or institutions that are recruiting investigators for clinical trials or other employment opportunities.

The popular mainstays that will be returning to the Exhibit Hall include Publishers' Row, where attendees can find relevant journals and textbooks; the New Exhibitor Pavilion, which will be filled with innovative products from companies not seen before at the ATS International Conference; and the ATS Public Advisory Roundtable (ATS PAR) row, featuring the 15 member organizations that represent individuals and families affected by lung diseases, critical illnesses and sleep disorders. Collectively, ATS PAR

provides the Society's Board of Directors with strategic guidance to keep the patient and family perspectives as a central focus of all ATS activities and programs.

"We encourage all attendees to visit the Exhibit Hall this year," said Michelle Turenne, director of ATS corporate alliances and development. "Whether you want more information on a new product or service, are interested in being an investigator in new clinical trials or want to talk with patients about various pulmonary diseases, the ATS 2009 Exhibit Hall has something that can benefit everyone who attends the ATS International Conference."

Product Theatres will be held Sunday-Tuesday over lunch in the Exhibit Hall. These are promotional programs that provide the latest information on specific drugs or devices. There are three Product Theatres in the Exhibit Hall, two of which seat 250 people and one that seats 150. Boxed lunches will be available to participants while quantities last. The *ATS Daily Bulletin* will publish a Product Theatre schedule each day, complete with topics and speakers.

"When exhibitors converse one-on-one in the booth, they can only interact with so many people," said Stacy Blackshaw, CEM, associate director of meetings and events at



The Exhibit Hall is an extension of the ATS 2009 educational experience, featuring nearly 200 companies showcasing products and services supporting pulmonary, critical care and sleep medicine.

Talley Management Group, Inc., a company that works with the ATS on the conference Exhibit Hall. "These Product Theatre presentations allow exhibitors to open the dialog to a much wider audience by having content experts talk about the latest information in specific therapeutic areas."

The Discovery Zone provides an opportunity to interact with participating exhibitors in some of the smaller booths throughout the Exhibit Hall, many of which have cutting-edge products or technology. Attendees will receive game cards in their registration packets, and the cards contain questions with answers that can only be found by visiting participating booths. Once cards are filled out with all questions correctly answered, attendees may place them in designated bins for daily prize drawings.

The Exhibit Hall's Recruitment Pavilion is a centralized area where ATS members and other attendees can talk to companies that are looking to recruit investigators for clinical trials. The pavilion will be located in the 2800 aisle on the right side of the Exhibit Hall.

"Everyone involved in pulmonary research is at the ATS meeting, so this is a great way to meet with potential investigators," said Robert K. Zeldin, M.D., vice president and U.S. medical franchise head of respiratory and dermatology at Novartis Pharmaceuticals Corporation.

Another enhancement involves more Internet booths. Those have always been available outside the Exhibit Hall, but as an extended service this year, another set of

see EXHIBIT HALL, page 8

ATS Forum to Focus on Diversity

The ATS annual Diversity Forum, which will take place from noon to 1:30 p.m. on Sunday, May 17, will highlight the importance of diversity within the fields of pulmonary, critical care and sleep medicine. The forum also serves as an opportunity to recognize the career advancement of minority group members.

This year, the forum will feature a special presentation by Wonder P. Drake, M.D., assistant professor of medicine in the Department of Infectious Diseases at Vanderbilt University School of Medicine, in Nashville. Dr. Drake will address the importance of increasing diversity within the research, academic and clinical realms to meet the needs of a diverse public.

The forum will also include the presentation of the 2009 ATS Minority Trainee Travel Awards (MTTAs). Supported by a generous grant from Merck & Co., Inc., the MTTA program recognizes junior researchers who co-authored abstracts accepted for presentation at the ATS International Conference

and who self-identify as an underrepresented minority, as defined by the National Institutes of Health. Each MTTA awardee will receive a grant, including one year's In-Training Membership, valued at \$75, and a check for \$1,425 to defray travel costs to the ATS International Conference. All past recipients are invited to attend the forum to share their experiences with the program and how it validated or changed their career paths.

Serving as Diversity Forum host will be Chadi A. Hage, M.D., assistant professor of medicine at the Veterans Administration Medical Center in Indianapolis. Dr. Hage is a member of the ATS Membership Committee, which develops the program for this annual event.

Conference badges are required for admission. Space is limited and admittance will be on a first-come, first-served basis. There is no additional fee, and a plated lunch will be served.

This event is supported by a grant from Merck & Co., Inc.

ATS 2009

continued from page 1

afternoon sessions are planned for Nursing Year in Review on Monday, May 18, and for Pediatrics Year in Review on Tuesday.

This year's President's Lecture features

Jeffrey Drazen, M.D., editor-in-chief of the *New England Journal of Medicine*, whose lecture is titled "In a Sea of Information, What Can We Trust?" Dr. Drazen will provide a thought-provoking review of challenges in obtaining information from basic, translational and clinical research and translating that information into clinical practice. Dr. Wright said. He will also offer perspectives on what it is like to be editor of the *NEJM*, a position he has held since 2000.

"Dr. Drazen has been an extremely insightful and forward-thinking leader on topics of how clinical practice is, and should be, affected by medical journals and how readers should consider concerns about conflict of interest in their reading of medical literature," Dr. Wright said. "The lecture

"The conference provides an outstanding blend of basic, clinical and translational science and up-to-date overviews of the state of the art in research and clinical care."

ATS President Jo Rae Wright, Ph.D.

will challenge us to think carefully about the sources of information that we have and how we incorporate that information into our daily routines."

This is just some of the first-rate programming and activities planned for ATS 2009 in San Diego.

"When it comes to meetings in our field, the ATS International Conference is regarded as one of the top meetings," Dr. Kraft said. "If people can only go to one meeting, they are likely to choose this one because it fulfills so many of their educational needs."

ATS PAR Symposium to Address Latest Advances in Pulmonary Fibrosis

During ATS 2009, the Society's Public Advisory Roundtable (PAR) will convene leading bench-to-bedside pulmonary fibrosis experts for its annual symposium from 1:30 to 4 p.m. on Sunday, May 17. The symposium will present basic science information, disease-specific scientific contributions, future directions for research and the patient perspective on pulmonary fibrosis.

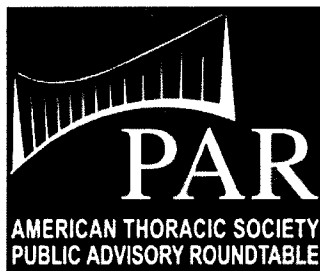
"The idea is to bring together clinicians, researchers and patients to examine carefully the current status of our understanding with pulmonary fibrosis," said ATS Immediate-Past President David H. Ingbar, M.D., professor of medicine and director of pulmonary and critical care at the University of Minnesota in Minneapolis, who will co-chair the symposium with Donna Appell, R.N.

"This session will include short talks from patients, who will put a face on this disease and add the patient perspective to the conversation," said Ms. Appell, ATS PAR chair.

The basic science review will include discussion of new fundamental mechanisms that lead to this usually idiopathic disease, including a mixture of genetic, occupational and environmental factors, Dr. Ingbar said.

A major symposium goal is to bring together knowledge about the common idiopathic types of pulmonary fibrosis with insights learned from more rare causes of familial pulmonary fibrosis. For example, researchers are particularly interested in pulmonary fibrosis as part of Hermansky-Pudlak Syndrome (HPS), whose causative molecular defect in the lungs is not as well understood as it is in the skin and other organs.

"The goal is to bring together the new mo-



lecular approaches, both in terms of identifying new targets for treatment based on our understandings of mechanisms and where we sit in terms of molecular diagnostics, biomarkers, proteomics and genomics," Dr. Ingbar said.

Recently, the first positive clinical trial outcome for idiopathic pulmonary fibrosis was reported using the drug pirfenidone. Now, eyes are on the pirfenidone clinical trial for HPS pulmonary fibrosis that is sponsored by the National Human Genome Research Institute (NHGRI).

"We will also talk about other clinical trials that are underway and new modalities for treatment, such as the potential application of stem cell therapy in these sets of diseases, and how they work," Dr. Ingbar continued.

Interactive discussion between speakers and the audience is a crucial feature of the ATS PAR symposium.

"It's a chance to discuss new directions in pulmonary fibrosis in a real out-of-the-box creative moment of anything new and anywhere we could head," Ms. Appell explained. "We want scientist and clinician attendees to be in the audience because we want their brilliant minds to be thinking about how to get us closer to curing pulmonary fibrosis."

Topics and speakers planned to date for this year's ATS PAR symposium include:

- "New Molecular Targets in Pulmonary Fibrosis," Peter B. Bitterman, M.D., professor of medicine and pulmonologist at the University of Minnesota in Minneapolis
- "Lessons From Pulmonary Fibrosis in Hermansky Pudlak Syndrome NHGRI," Bernadette Gochuico, M.D., pulmonary investigator at the National Human Genome Research Institute in Bethesda, Maryland
- "Genomics and Pulmonary Fibrosis," James E. Loyd, M.D., the Rudy W. Jacobson professor of medicine in the Department of Medicine/Division of Allergy, Pulmonary and Critical Care Medicine at Vanderbilt University School of Medicine in Nashville, Tennessee
- "Molecular Diagnostics and Biomarkers in IPE," Naftali Kaminski, M.D., director of the Dorothy P. and Richard P. Simmons Center for Interstitial Lung Disease in the Division of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh in Pennsylvania
- "Where Are We With Clinical Trials in IPE?" Paul W. Noble, M.D., chief of the Division of Pulmonary, Allergy, and Critical Care at Duke University in Durham, North Carolina
- "Novel Treatments for Pulmonary Fibrosis: Stem Cells and All That Jazz," Luis A. Ortiz, M.D., associate professor in the Division of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh in Pennsylvania

Pick Up Complimentary Journals, Magazines at ATS 2009

This year, the American Thoracic Society is offering attendees an additional benefit for registering for the ATS 2009 International Conference—the opportunity to pick up copies of leading medical journals and news magazines, free-of-charge, during the conference.

The following periodicals will be available at the ATS 2009 Journal Annex, located outside of the Exhibit Hall in the San Diego Convention Center:

- *American Journal of Respiratory and Critical Care Medicine*
- *American Journal of Respiratory Cell and Molecular Biology*
- *Canadian Respiratory Journal*
- *Clinical Respiratory Journal*
- *Journal of Physiology*
- *Journal of the American Medical Association*
- *Journal of Sleep Research*
- *New England Journal of Medicine*
- *Proceedings of the American Thoracic Society*
- *Science*
- *The Lancet*
- *Thorax*

New this year, a number of leading news magazines that cover the fields of respiratory, critical care and sleep medicine will also be available at a designated area outside of the Exhibit Hall.

Attendees may pick up free copies of the following publications at the ATS 2009 Magazine Annex:

- *Advance for Managers of Respiratory Care*
- *Advance for Respiratory Care Practitioners*
- *Pulmonary Reviews*
- *RT for Decision Makers in Respiratory Care*

ATS 2009 Offers Exceptional Programs Presented in Myriad Formats

Among the interactive courses, symposia and workshops at ATS 2009 are PG 17: "Interventional Pulmonology with Practical Demonstration: Something for Every Pulmonologist," WS1: "Endobronchial Ultrasound," A11: Fellow Case Conference: Third Edition, B12: "Fellows Symposium: Practical Tips for Transitioning to a Successful Academic Career" and WS4 "Bronchiectasis: Many Causes, Shared Challenges."

PG 17, which will take place from 8 a.m. to 4 p.m., on Saturday, May 16, will "update the audience on interventional pulmonology technologies already in use and familiarize attendees with new technologies, such as electromagnetic navigation and endobronchial ultrasound," said course chair Praveen N. Mathur, M.B.B.S., professor of clinical medicine at Indiana University School of Medicine in Indianapolis. "This course also provides a knowledge base to those pulmonologists who may want to secure more training in specific techniques and technologies. This course would cement their interest."

WS1, scheduled from noon to 1:30 p.m., on Sunday, May 17, will demonstrate how endobronchial ultrasound provides real-time feedback.

"Endobronchial ultrasound has become a very mature technology, and it has proven valuable in staging lung cancer," said workshop chair Armin Ernst, M.D., director of interventional pulmonary at Beth Israel Deaconess Medical Center in Boston. "In this session, we will discuss the applications and also provide a hands-on feature using models for participants to try out this new and exciting technology."

A11, on the other hand, "pits some of the best minds in pulmonary medicine, radiology and pathology against a series of fascinating clinical cases," said session chair John G. Mastrorade, M.D., chair of the ATS Training Committee and associate professor at Ohio State University in Columbus. "The real attraction of the Fellow Case Conference is to observe how master physicians work their way through these challenging clinical scenarios." He notes that both fellows and senior clinicians and

researchers are encouraged to attend this session, which will take place from 8:15 to 10:45 a.m. Sunday, May 17.

B12 on academic careers offers a "summary of current economic realities and opportunities and practical advice on the nuts and bolts of achieving success in academia," said course chair Robert Kempainen, M.D., associate professor of medicine at University of Minnesota School of Medicine in Minneapolis. The course, scheduled from 8:15 to 10:45 a.m., on Monday, May 18, will serve as a great supplement to the advice attendees are receiving at their home institutions.

WS4 will provide an update on the different causes of bronchiectasis and will cover the epidemiology and treatment of cystic fibrosis, primary ciliary dyskinesia, immune deficiency and infections. The workshop, which will be held from noon to 1:30 p.m., on Monday, May 18, will also address similarities and differences of effective treatments for different causes of bronchiectasis.

These courses join scores of educational



Marvin I. Schwarz, M.D., served as one of the expert panelists for last year's case-based sessions that focused on clinical pulmonologists, critical care physicians, hospitalists and trainees in pulmonary and critical care medicine.

programs addressing the most relevant topics in the field.

"This year's International Conference will offer high-quality science," said conference committee chair Monica Kraft, M.D. "We will feature the authorities in the field and provide attendees with an opportunity to interact with experts."

Assembly Leaders Highlight Not-To-Be-Missed Presentations

The American Thoracic Society's 13 assemblies have highlighted these abstracts as some of the most interesting to be presented at ATS International Conference in San Diego. Search for full abstracts by title, author or session at www.abstracts2view.com/ats09 in late April.

Assembly on Allergy,

Immunology and Inflammation

"Deletion of Myeloid Cell I- κ B Kinase B Prevents Induction of Mouse Lung Allergic Tolerance." **Authors:** H.J. Huang, S. Sugimoto, G.A. Patterson, A.S. Krupnick, D. Kreisel, A.E. Gelman, St. Louis, Missouri. **Session:** B91 "The Yin and Yang of Lung Injury: New Insights into Mechanisms of Progression and Resolution" (*Mini-Symposium; 1:30 to 4 p.m., Monday, May 18, Room 3, Upper Level, San Diego Convention Center*)

"Localization and Enumeration of Human Lung Dendritic Cells from Asthmatic Patients Undergoing Anti-IgE Therapy: A Multispectral Confocal Microscopy Study." **Authors:** H.S. Chand, M. Schuyler, M.E. Lipscomb, Albuquerque, New Mexico. **Session:** C13 "Mechanisms of Disease in Human Asthma" (*Mini-Symposium; 8:15 to 10:45 a.m., Tuesday, May 19, Room 33 A-C, Upper Level, SDCC*)

Assembly on Behavioral Science

"Improving Asthma Care for Minority Children in Head Start (HS)." **Authors:** A.L. Billerback, M.N. Eakin, K.A. Butz, M.E. Bollinger, C.S. Rand, K.A. Riekert, Baltimore, Maryland. **Session:** B14 "Pediatric Asthma: Opportunities and Challenges to Improving Outcomes" (*Mini-Symposium; 8:15 to 10:30 a.m., Monday, May 18, Room 7 A-B, Upper Level, SDCC*)

"Environmental Tobacco Smoke Exposure in Childhood Predicts Early Emphysema in Adulthood: The MESA Lung Study." **Authors:** G.S. Lovasi, A.V. Diez-Roux, E.A. Hoffman, R. Jiang, D.R. Jacobs, S. Kawut, R.G. Barr, Iowa City, IA, Ann Arbor, Michigan; Minneapolis, Minnesota; New York, New York. **Session:** C17 "Smoking Cessation" (*Mini-Symposium; 8:15 to 10:45 a.m., Tuesday, May 19, Room 30 A-B, Upper Level, SDCC*)

Assembly on Clinical Problems

"The CAPACITY (CAP) Trials: Randomized, Double-Blind, Placebo-Controlled, Phase III Trials of Pirfenidone (PFD) in Patients with Idiopathic Pulmonary Fibrosis (IPF)." **Authors:** P. Noble, C. Albera, W. Bradford, U. Costabel, D. Kardatzke, T. King, Jr., S. Sahn, J. Szwarcberg, D. Valeyre, R. du Bois, Brisbane, San Francisco, California; Denver, Colorado; Durham, North Carolina; Charleston, South Carolina; Paris, France; Essen, Germany; and Italy. **Session:** A23 "Interstitial Lung Disease: Outcomes and Selected Clinical Issues" (*Poster Discussion Session; 8:15 to 10:45 a.m., Sunday, May 17, Room 6 F, Upper Level, SDCC*)

"The (Cost)-Effectiveness of Self-Treatment of Exacerbations on the Severity of Exacerbations in COPD Patients: The COPE II-Study." **Authors:** T.W. Effing, H.A.M. Kerstjens, P.D.L.P.M. van der Valk, G.A. Zielhuis, J. van der Palen, Enschede, Groningen, Nijmegen, The Netherlands. **Session:** A39 "Chronic Obstructive Pulmonary Disease Exacerbations" (*Thematic Poster Session; 8:15 a.m. to 4 p.m., Sunday, May 17, Area K, Sails Pavilion, Upper Level, SDCC*)

Assembly on Critical Care

"Effect of Race on the Incidence of Acute Lung Injury." **Authors:** S.E. Erickson, C.R. Cooke, M.D. Eisner, G.S. Martin, Atlanta, Georgia; Seattle, Washington; San Francisco, California. **Session:** C92 "Acute Lung Injury/ Acute Respiratory Distress Syndrome: Outcomes And Predictors Of Failure" (*Mini-Symposium; 1:30 to 4 p.m., Tuesday, May 19, Room 30 C-E, Upper Level, SDCC*)

"Plateau Pressure: A Lung-Specific Predictor of Hospital Mortality in Patients with Acute Lung Injury (ALI)." **Authors:** W. Checkley, D. Hager, R. Brower, Baltimore, Maryland. **Session:** C92 "Acute Lung Injury/ Acute Respiratory Distress Syndrome: Outcomes and Predictors of Failure" (*Mini-Symposium; 1:30 to 4 p.m., Tuesday, May 19, Room 30 C-E, Upper Level, SDCC*)

Assembly on Environmental & Occupational Health

"A Carbon Nanotube Model of Pulmonary Granuloma in Wild-Type and PPAR γ Knock Out (KO) Mice." **Authors:** D. Brescia, L. Dobbs, C.J. Kungold, B.P. Barna, A.J. McCoy, A. Malur, C. Winkoly, M.S. Kavuru, M.J. Thomassen, Greenville, North Carolina. **Session:** C105 "Nanomaterials: Little Particles, Big Impact" (*Poster Discussion Session; 1:30 to 4 p.m., Tuesday, May 19, San Diego Ballroom B, North Tower, Lobby Level, San Diego Marriott Hotel And Marina*)

"A High Fat, High Energy Food Challenge Induces an Exaggerated Inflammatory Response in Asthma." **Authors:** L.G. Wood, M.L. Garg, A. Wood, J. Smart, P.G. Gibson, Newcastle, Australia. **Session:** A94 "Asthma as a Systemic Disease: The Role of Co-Morbidities" (*Mini-Symposium; 1:30 to 4 p.m., Sunday, May 17, Room 6 C, Upper Level, SDCC*)

Assembly on Microbiology, Tuberculosis & Pulmonary Infections

"Extensively Drug-Resistant Tuberculosis—A Threat to Health Care Workers." **Authors:** J.M. Jarand, M. Loveday, K. Shean, P. Wilcox, K. Dheda, Calgary, Canada, Cape Town, Western Cape, South Africa. **Session:** A96 "Tuberculosis: Assessing Transmission and Risk" (*Mini-Symposium; 1:30 to 4 p.m., Sunday, May 17, Room 33 A-C, Upper Level, SDCC*)

"Zinc Supplementation Restores GM-CSF Signaling in the Alveolar Macrophage and Facilitates Clearance of Klebsiella Pneumoniae in the Lungs of Alcohol-Fed Rats." **Authors:** A.J. Mehta, P.C. Joshi, X. Fan, D.M. Guidot, Atlanta, Georgia. **Session:** A15 "Pulmonary Infections: Modulating Host Defenses" (*Mini-Symposium; 1:30 to 10:45 a.m., Sunday, May 17, Room 11 A-B, Upper Level, SDCC*)

Assembly on Nursing

"Effect of Oral Corticosteroid Addiction in Treatment of Controlled Asthma Patients: A Randomized Clinical Trial." **Authors:** A.A. Araruna, M.M. Amorim, L.B. Caetano,

I.L. Santoro, A.L.G. Fernandes, São Paulo, Brazil. **Session:** A16 "Asthma Management/ Monitoring Chronic Obstructive Pulmonary Disease" (*Mini-Symposium; 8:15 to 10:45 a.m., Sunday, May 17, Room 3, Upper Level, SDCC*)

"Environmental Tobacco Smoke Exposure in Childhood Predicts Early Emphysema in Adulthood: The MESA Lung Study." **Authors:** G.S. Lovasi, A.V. Diez-Roux, E.A. Hoffman, R. Jiang, D.R. Jacobs, S. Kawut, R.G. Barr, Iowa City, IA, Ann Arbor, MI, Minneapolis, MN, New York, NY. **Session:** C17 "Smoking Cessation" (*Mini-Symposium; 8:15 to 10:45 a.m., Tuesday, May 19, Room 30 A-B, Upper Level, SDCC*)

Assembly on Pediatrics

"Immune Response Varies by TLR4 Genotype After RSV Infection." **Authors:** T.W. Guilbert, S.A. Sund, M.D. Evans, C. Ober, J.E. Gern, R.F. Lemanske, Jr., Madison, Wisconsin; Chicago, Illinois. **Session:** C94 "Viral Infections in Childhood Respiratory Disease" (*Mini-Symposium; 1:30 to 4 p.m., Tuesday, May 19, Room 3, Upper Level, SDCC*)

"Anti-IL-5 Treatment Attenuates the Asthma Phenotype in Infant Monkeys, But Also Affects Normal Lung Development." **Authors:** J.A. Miller, J.E. Gerriets, R.O. Fishman, E.D. Wallis, K.P. Maniar, J.H. Fontaine, E.S. Bestelegue, California. **Session:** A97 "Be in Pediatrics" (*Mini-Symposium; 1:30 to 4 p.m., Sunday, May 17, Marriott Hall 3, SDMHM*)

Assembly on Pulmonary Circulation

"A Primary Role of Activated CD8+ T-Cells in the Pathogenesis of Pulmonary Arterial Hypertension." **Authors:** G. Sutendra, S. Bonnet, P. Dromparis, S. McMurtry, A. Haromy, C. Bleackley, E.D. Michelakis, Edmonton, Canada. **Session:** A106 "Role of Inflammation in Pulmonary Vascular Remodeling and Injury" (*Poster Discussion Session; 1:30 to 4 p.m., Sunday, May 17, Room 8, Upper Level, SDCC*)

"Prevalence and Mechanism of Pulmonary Hypertension in Sickle Cell Disease: A Prospective Multicenter French Study." **Authors:** F. Parent, D. Bachir, F. Lionnet, J. Inamo, F. Driss, L. Savale, G. Loko, A. Elmazouzi, A. Letierce, R. Girot, F. Galacteros, G. Simonneau, Clamart, France. **Session:** B27 "From Alpha to Omega: Assessment and Outcomes in Pulmonary Hypertension" (*Poster Discussion Session; 8:15 to 10:45 a.m., Monday, May 18, Room 31 A-C, Upper Level, SDCC*)

Assembly on Pulmonary Rehabilitation

"Cost-Effectiveness of a 24-Month INTERdisciplinary COMMunity-Based COPD Management Program (INTERCOM) in Patients with Less Advanced Airflow Obstruction." **Authors:** C.R. van Weetering, M. Hoogendoorn, D.R. De Munck, M.P. Rutten-van Molken, A.M. Schols, Veldhoven, Rotterdam, Maastricht, The Netherlands. **Session:** D16 "Outcomes in Pulmonary Rehabilitation" (*Mini-Symposium; 8:15 to 10:45 a.m., Wednesday, May 20, Room 6 E, Upper Level, SDCC*)

"Contractile Muscle Fatigue is Associated with Effectiveness of Exercise Training in COPD." **Authors:** C. Burtin, D. Saeys, D. Langer, M. Saglam, R. Gosselink, M. Decramer, T. Troosters, Leuven, Belgium. **Session:** A18 "Pulmonary Rehabilitation: Adding Muscle to Therapy for Patients with Respiratory Disease" (*Mini-Symposium; 8:15 to 10:45 a.m., Sunday, May 17, Room 30 C-E, Upper Level, SDCC*)

Assembly on Respiratory Cell and Molecular Biology

"On the TRAIL of a Killer: TRAIL-Expressing Mesenchymal Stem Cells are Able to Target and Eliminate Lung Metastases." **Authors:** M.R. Loebinger, S.M. Janes, London, England. **Session:** C96 "Lung Tumorigenesis: Insights from Animal Models" (*Mini-Symposium; 1:30 to 4 p.m., Tuesday, May 19, Marriott Hall 5-6, SDMHM*)

"Dimethylarginine Dimethylaminohydrolyase 2 in Idiopathic Pulmonary Fibrosis." **Authors:** S.S. Pullamsetti, R. Savai, R. Dumitrascu, M. Konigshoff, H.A. Ghofrani, N. Weissmann, F. Grimminger, O. Eickelberg, A. Guenther, J. Leiper, W. Seeger, R.T. Schermuly, Giessen, Bad Nauheim, Germany, London, England. **Session:** D17 "Fibroblasts, Progenitor Cells and Models of Interstitial Fibrosis that Reveal Mechanisms of Disease" (*Mini-Symposium; 8:15 to 10:45 a.m., Wednesday, May 20, Marriott Hall 4, SDMHM*)

Assembly on Respiratory Structure and Function

"Allogeneic Human Mesenchymal Stem Cells Improve Endothelial Barrier Integrity Across Human Lung Microvascular Endothelial Cells Following an Inflammatory Insult." **Authors:** J.W. Lee, J. Howard, M.A. Matthay, San Francisco, California. **Session:** B97 "Mesenchymal Stem Cells in the Lung: Recruitment, Retention and Performance" (*Mini-Symposium; 1:30 to 4 p.m., Monday, May 18, Room 30 A-B, Upper Level, SDCC*)

"Non-Destructive Morphometric Assessment of Murine Acinus Via Hi-Res microCT." **Authors:** D.M. Vasilescu, D. Chon, T. Fong, J. Heverhagen, M. Ochs, E.R. Weibel, E.A. Hoffman, Concord, CA, Iowa City, IA, Marburg, Germany, Bern, Switzerland. **Session:** A19 "Imaging the Distal Lung: Advances in Technique and Application" (*Mini-Symposium; 8:15 to 10:45 a.m., Sunday, May 17, Room 1 A-B, Upper Level, SDCC*)

Assembly on Sleep and Respiratory Neurobiology

"Intermittent Hypoxia Alters Endothelial Cell Barrier Function: Role of ROS and MAP Kinases." **Authors:** M.M. Lee, V. Makarenko, J. Nanduri, P. Usatyuk, V. Natarajan, N.R. Prabhakar, Chicago, Illinois. **Session:** A20 "Physiological Responses to Intermittent Hypoxia" (*Mini-Symposium; 8:15 to 10:45 a.m., Sunday, May 17, Marriott Hall 4, San Diego Marriott Hotel and Marina*)

"Obesity, Leptin and Upper Airway Collapsibility in Mice." **Authors:** A.S. Elsayed-Ahmed, L.E. Pichard, H. Schneider, P.L. Smith, V. Polotsky, A.R. Schwartz, Baltimore, Maryland. **Session:** D19 "Upper Airway: State of the Art 2009" (*Mini-Symposium; 8:15 to 10:45 a.m., Wednesday, May 20, Room 11 A-B, Upper Level, SDCC*)

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Meet Future Clinicians, Researchers, Educators at Exchange

The Fellow and Junior Professional Exchange is an annual networking event at the ATS International Conference for pulmonary, critical care and sleep medicine fellows, internal medicine and pediatric residents and other trainees, as well as for those transitioning to professional careers. The 2009 exchange will take place from 7 to 8 p.m. on Sunday, May 17.

This informal, resource-filled event allows trainees and others at the beginning of their careers to network with peers and leaders in their fields. This year, the exchange will feature career pathway experts who will discuss their professional journeys in pulmonary, critical care and sleep medicine from a variety of perspectives at the "bench and bedside"—including research, academia, administration and clinical practice.

ATS leaders, program directors, national public health experts and decision-makers look forward to this exchange as an opportunity to meet and greet future clinicians, researchers and educators.

Each year, this event is jointly developed and hosted by the ATS Membership Committee, Training Committee and Members In-Transition and Training Committee.

Conference badges are required for admission. Space is limited and admittance will be on a first-come, first-served basis. There is no additional fee. Cocktails and hors d'oeuvres will be served.

RESEARCH

continued from page 1

findings for the audience to understand what we have found to date about factors that contribute to the development of allergy and wheezing disease in inner-city infants."

Hear how NASA is in a unique position to contribute to pulmonary science during the session "Moon Dust and Pollen: Initial Results of Exploratory Research with NASA" from noon to 1 p.m. on Monday, May 18. The NASA-sponsored session will address recent research on the hazards of the super-fine moon dust and opportunities to track by satellite seasonal concentrations of pollen.

"I hope attendees will learn that this is another way to understand the distribution of pollen and areas of asthma exposure, and to realize that longer moon explorations will result in more danger from moon dust to astronauts and the need to protect them from that," said session co-chair William C. Bailey, M.D., professor of medicine at the University of Alabama at Birmingham. "I also hope attendees will make contacts with NASA researchers to learn more about opportunities to participate in such research."

During the "Long-Term Outcomes from the Inhaled Nitric Oxide Trials in Neonates" session from noon to 1 p.m. on Sunday, May 17, the results of two NHLBI-funded trials and of one industry-sponsored trial will be presented. All examined long-term outcomes of chronic lung disease, cost effectiveness and neurodevelopmental disability one to four years after treatment.

"The indications, benefits and risks of iNO therapy in preterm infants are important and may lead to changes in the way neonatologists manage preterm infants at risk of bronchopulmonary dysplasia, or BPD, as well as influence the long-term

outcomes of these infants as evaluated by pulmonologists, pediatricians and neurologists," said session co-chair Carol J. Blaisdell, M.D., medical officer of Lung Developmental Biology and Pediatric Pulmonary Diseases in the Division of Lung Diseases at the NHLBI. "The results from these studies will contribute to the evidence base to develop practice guidelines for treating the preterm infant with iNO."

To promote pulmonary research efforts, the ATS Assembly on Nursing will sponsor a research session on "National Institute of Nursing Research (NINR): Funding Opportunities and Priorities" from noon to 1 p.m. on Sunday, May 17.

The ATS International Conference attracts many nurse researchers who have been funded by the NINR or other NIH institutes and those who are in a position to apply for grants and funding, said session chair Lynn F. Reinke, Ph.D., A.R.N.P., a research fellow in Health Services R&D and advance practice nurse at the Department of Veterans Affairs in Seattle.

"This venue is a perfect opportunity for NINR program officers to personally convey the NIH agenda and funding priorities," Dr. Reinke said. "The funding opportunities from NINR often focus on methods to improve clinical care for patients with lung disease. Hence, the majority of research conducted by nurse investigators directly translates to good quality patient-care outcomes."

Other noteworthy research topics at ATS 2009 will be presented during the following times and days:

Noon to 1 p.m., Sunday, May 17

L2: "Update on Training and Use of Spirometry in Occupational Settings"

L4: "NHLBI Asthma Clinical Research Network (ACRN) and Chronic Obstructive Pulmonary Disease Clinical Research

Network (CCRN): New Findings"

L6: "The Biology of Asthma Disparities: Findings from the NHLBI Centers for Reducing Asthma Disparities"

Noon to 1 p.m., Monday, May 18

L9: "The Coronary Artery Risk Development in Young Adults (CARDIA) Study: Insights into Lung Disease and Lung Function in Young Adults"

L10: "Using Genetic and Genomic Technologies to Better Understand Asthma: New Findings from the NHLBI Clinical Research Programs"

L11: "Acute Respiratory Distress Syndrome Network (ARDSNet): Results of the Albuterol for the Treatment of Acute Lung Injury (ALTA) Trial"

L12: "Cardiovascular and Other Health Consequences of Sleep-Disordered Breathing and Hypoxia in Older Men"

Noon to 1 p.m., Wednesday, May 20

L13: "Chronic Obstructive Pulmonary Disease Outcomes Based Network for Clinical Effectiveness and Research Translation (CONCERT Consortium)"

L14: "Clinical Implications of Acid Reflux: Therapy and Rhinosinusitis in Asthma: Results from the ALA Asthma Clinical Research Centers"

L15: "Update from the CDC's Tuberculosis Trails and Tuberculosis Epidemiological Studies Consortium"

L16: "Translational Research Efforts on Pulmonary Disease and Genetic Susceptibility to Air Pollution"

L17: "Idiopathic Pulmonary Fibrosis Network: New Insights into IPF Pathogenesis and Therapy"

L18: "The Multi-Ethnic Study of Atherosclerosis: Investigation of Cardiopulmonary Interactions in Adults"


L19: "NHLBI Cultural Competence and Health Disparity Academic Award Program for Pulmonary Medicine"

Fully Paid Registrants May Access ATS 2009 Webcasts

As a benefit of registering for the American Thoracic Society's 2009 International Conference, the ATS is again offering 12 months of free access to ATS 2009 IC Webcasts. Fully paid conference registrants will have post-meeting access to more than 200 hours of ATS 2009 presentations, reflecting the diverse topic areas of the conference at no extra charge.

The "Best of ATS Conferences" Webcasts provide full audio and slides, synchronized and searchable. More details will be provided in the ATS International Conference final program and onsite materials.

Free access is limited to paid conference registrants in full conference categories (including in-training). One-day registrants, other attendees and non-attendees may pay for this 12-month access by placing orders at designated pricing levels to be announced in the final program onsite.



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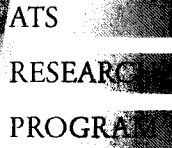
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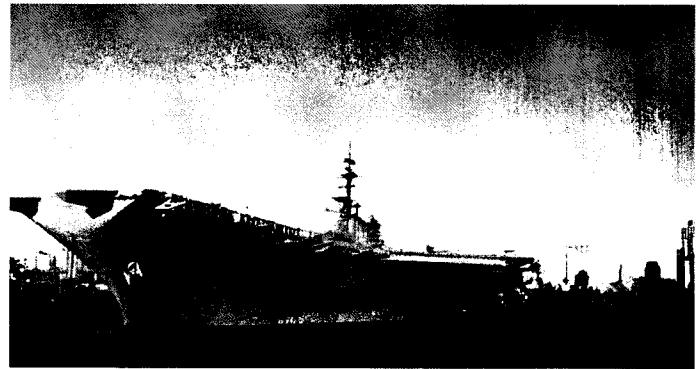
San Diego consistently ranks as one of the top travel destinations in North America because of its picture-perfect landscape and exceptional attractions. The region is home to 33 beaches, and plenty of scenic stops offer breath-taking views of the Pacific Ocean's blue waters. Each day, tourists flock to San Diego's scenic locales, museums and distinctive shops and boutiques. Enjoy the best San Diego has to offer by taking a tour during the American Thoracic Society's 2009 International Conference. For more information about these tours or to register online, visit www.thoracic.org/go/international-conference.

- The San Diego Orientation tour will provide an overview of not-to-be missed attractions at no charge. (Friday, May 15, 9:30 to 10 a.m.)
- The San Diego City Tour with Harbor Cruise will begin at Balboa Park, the horticultural wonder in the heart of San Diego. Guests will then take a 21-mile cruise on San Diego Bay, one of the most beautiful natural harbors in the world. (10 a.m. to 3 p.m., Friday, May 15, and Tuesday, May 19; \$43/person)



Torrey Pines Golf Course

- The La Jolla Tour takes visitors to this scenic seaside village, located on seven spectacular miles of sandy beaches and stunning cliffs. La Jolla is home to upscale boutiques, chic restaurants, the Stephen Birch Aquarium & Museum and the San Diego Museum of Contemporary Art. (11 a.m. to 3 p.m., Friday, May 15, and 1 to 5 p.m., Sunday, May 17; \$26/person)
- The Midway Tour with Harbor Cruise begins with exploring this former U.S. Navy aircraft carrier, which has been converted into a multi-dimensional museum. Next guests embark upon a 21-mile cruise of scenic waterways, including Harbor and Shelter Islands, Point Loma (home of the Cabrillo Monument), the magnificent Coronado Bay Bridge and the U.S. Pacific Naval Fleet. (10 a.m. to 3 p.m. Saturday, May 16, and Wednesday, May 20; \$62/person)
- The Shopping in Del Mar and Solana Beach tour includes a special afternoon of browsing lovely shops at Del Mar Plaza and the neighboring area—and then goes on to



Midway Museum

- the shops of the Cedros Design District in Solana Beach, which is known for antiques and designer and specialty items. (10:30 a.m. to 3:30 p.m., Saturday, May 16; \$30/person)
- The Coronado Walking Tour begins at the clock tower of the famous, century-old Hotel del Coronado. From "The Dell," the tour then continues to some of the island's magnificent celebrity homes. Depending on interests, guests may later visit either quaint shops, cafes and galleries or stroll along the sandy Coronado Beach, the best seashell beach in San Diego. (1 to 5 p.m., Saturday, May 16, and 10 a.m. to 2 p.m., Monday, May 18; \$45/person)
- The Wild Animal Park Tour takes visitors to the 2,100-acre sanctuary, where animals roam freely in settings similar to their native African and North American habitats. The park features a special open-air tram with an informative guide describing the park's animals. (11 a.m. to 4 p.m., Sunday, May 17, and Tuesday, May 19; \$64/person)
- The Southern California Wine Tour includes a visit and tasting at one winery and a tasting at a second winery in the wine-famous Temecula Valley. Temecula Valley has become renowned for producing everything from vintage sherry to award-winning champagne. (9 a.m. to 3 p.m., Monday, May 18; \$75/person)
- The Aolani Catamaran Cruise offers the smoothest ride on the San Diego Bay, with spectacular scenery of the San Diego skyline and the bay's majestic waters. The 31-foot catamaran accommodates up to 30 people, and guests can walk freely around the boat. (1 to 5 p.m., Monday, May 18; \$113/person)
- The Trekking in Torrey Pines tour features an invigorating day of hiking in the scenic Torrey Pines State Reserve, perched high atop the bluffs overlooking the Pacific Ocean. The reserve offers breathtaking views, superb trails and gnarled, twisted, rugged Torrey pine trees. (1 to 5 p.m., Tuesday, May 19; \$47/person)

MECHANICAL VENTILATION continued from page 3

in mechanical ventilation," said Niall D. Ferguson, M.D., M.S.C., who co-chairs the PG6 course. "It will also include an extensive discussion on non-invasive ventilation (NIV), a rapidly expanding technology about which clinicians want to learn more."

The course will additionally address the latest innovations in three modes of ventilation—proportional assist ventilation, neurally adjusted ventilatory assistance and high-frequency ventilation, said Dr. Ferguson, director of clinical research in critical care medicine at the University of Toronto. It will end with disease-specific discussion on pediatric patients, airway obstruction in asthma and COPD, acute lung injury and acute respiratory distress syndrome.

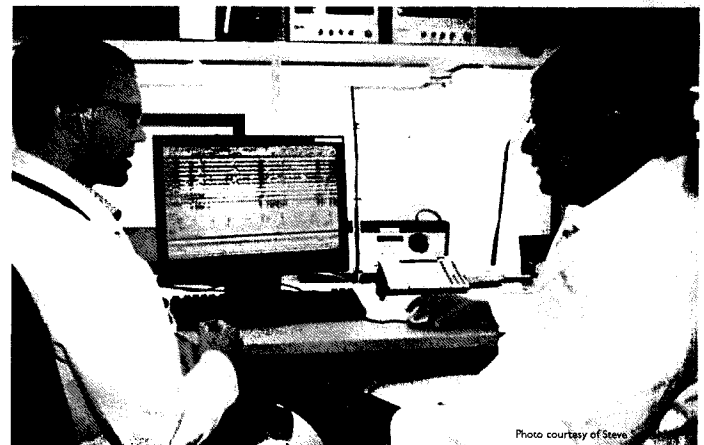
PG20: "Weaning from Mechanical Ventilation" will cover the pathophysiology of weaning failure and the role of respiratory muscles, the potential use of the various weaning predictors, the role of weaning protocols and the utility of

automated weaning techniques, the role of non-invasive ventilation in weaning failure, and post-extubation failure and the clinical approach to managing the difficult to wean patient. Dr. Nava also co-chairs this course with Franco Laghi, M.D., professor of medicine, pulmonary and critical care medicine at Ed Hines Jr., VA Hospital and Loyola University Medical Center, in Hines, Ill., and Theodoros Vassilakopoulos, M.D., of the Department of Critical Care and Pulmonary Services at the University of Athens Medical School and Evangelismos Hospital in Greece.

"There are still so many differences around the world regarding the practice of mechanical ventilation and weaning," Dr. Nava said. For example, weaning protocols are popular in the U.S., but not so popular in Europe. Nevertheless, "overall our clinical success is very similar."

It may be easier to convince a physician to change their prescribing practices of a drug than to change modes of ventilation that they are comfortable with, he said.

"Honestly, very few drugs influence



Two sleep medicine clinicians conduct a study on sleep tracing used to diagnose sleep disorders. Sleep disorders and sleep neurobiology and physiology will be addressed during the sleep medicine postgraduate courses.

outcomes on patients as much as a well-applied ventilatory strategy," Dr. Nava said. "By reviewing the most recent advances

and guidelines, these courses will be helpful in driving our colleagues toward new attitudes."

CURRENT AND EMERGING THERAPIES FOR PAIN

Current Challenges, Fresh Approaches

Evening Postgraduate
Seminar

May 17, 2008

San Diego, California

Dinner - 6:30pm

Program - 7:00-9:00pm

Manchester Grand Hyatt Hotel

Exhibition Galleries E-11

Session Code - E1



The Joint for world leaders
PAIN MEDICINE • 100 YEARS OF PAIN



GILEAD

Improving patient outcomes
through science and innovation



Current Controversies in Pulmonary Arterial Hypertension: **PRO-CON DEBATES**



PROGRAM

**7:30 am PPH: Starting and Picking the Best
App Patient and Agents**
Sean P. Galine, MD, PhD
Mater Misericordiae
University Hospital
University College Dublin
Dublin, Ireland

**7:35 am EPP: Traditional and Picking the Best
Bids for Health Agents. The Need for
Best Picking for Long-Term Mortality
and Morbidity**
Victor F. Tapson, MD
Duke University Medical Center
Durham, North Carolina

7:50 am GENERAL SESSION

**7:40 am PPH: Combination Therapy to
Effectiveness and Recommendations of
for Most PH Patients**
Valerie Y. McLaughlin, MD
University of Michigan
Health System
Ann Arbor, Michigan

**7:55 am EPP: How to Use Endpoints to
Rationally Assess Combination
Therapy for the Treatment of PH**
David B. Badesch, MD
University of Colorado Health
Sciences Center
Aurora, Colorado

8:10 am GENERAL SESSION

**8:20 am PPH: Oral and Inhaled PH
Therapies Are Highly Effective for
Most Patients, Preserving the Need
for Parental Therapy**
Lewis J. Rubin, MD
UCSD School of Medicine
La Jolla, California

**8:25 PM-8:55: Oral and Inhaled PH Therapies Are
Indispensable for Many Patients. First-Line
Parenteral Parenteral Therapy Should Be
One of Many Options**
Robyn J. Barst, MD
Columbia University College of
Physicians and Surgeons
New York, New York

8:50 am GENERAL SESSION



Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Wednesday, February 03, 2010 10:31 AM
To: Gantz, Marie; Wally Carlo, M.D.
Cc: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: SUPPORT revision progress

Understood
Thanks
Neil

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Wednesday, February 03, 2010 7:15 AM
To: Finer, Neil; Wally Carlo, M.D.
Cc: Das, Abhik; Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT revision progress

Hi Neil and Wally,

I wanted to let you know that I will be responding to your requests for the NEJM revisions later this week. Just to fill you in, I've been made PI of one of our other DCC projects following the recent death of one of our RTI colleagues, and I've been in the Rockville office this week taking care of some urgent issues for that project. But I know the NEJM revisions are very high priority, and I will be working on them tomorrow and Friday.

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Wally Carlo, M.D."
Subject: RE: Support
Date: Tuesday, February 02, 2010 2:07:00 PM

She has some – we will work with the NEJM editorial assistant (Brendan Abel) and get it done

Thanks
Rose

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Sunday, January 31, 2010 8:31 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: RE: Support

Maybe Stephanie can send reminders to those who have not sent them in. I think NEJM is trying to get the paper published soon and we don't want this to delay them.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Sun 1/31/2010 5:11 PM
To: Wally Carlo, M.D.; 'nfiner@ucsd.edu'; 'adas@rti.org'; 'mgantz@rti.org'; 'wrich@ucsd.edu'
Cc: 'mcunningham@rti.org'
Subject: Re: Support

I had sent the forms out - we have many of them already

Rose

From: Wally Carlo, M.D. <WCarlo@peds.uab.edu>
To: Higgins, Rosemary (NIH/NICHD) [E]; nfiner@ucsd.edu <nfiner@ucsd.edu>; adas@rti.org <adas@rti.org>; mgantz@rti.org <mgantz@rti.org>; wrich@ucsd.edu <wrich@ucsd.edu>
Cc: Cunningham, Meg <mcunningham@rti.org>
Sent: Sun Jan 31 18:05:17 2010
Subject: RE: Support

We need the disclosure forms of each author so we can do the one that goes in the paper. I checked the instructions on the web and can do the first draft (for both papers) once I get all forms or someone else can do it for both papers.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thu 1/28/2010 12:41 PM
To: Wally Carlo, M.D.; nfiner@ucsd.edu; adas@rti.org; mgantz@rti.org; wrich@ucsd.edu
Cc: Cunningham, Meg
Subject: RE: Support

Neil is not attending (though this would be great if he could attend. We could see if there is any time - Meg - can you look at the agenda and see if there is a time possible for SUPPORT Subcommittee?? Perhaps before the dinner on 2/11?

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, January 28, 2010 1:39 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; wcarlo@peds.uab.edu; nfiner@ucsd.edu; adas@rti.org; mgantz@rti.org;
wrich@ucsd.edu
Subject: RE: Support

We will be at the NRN meeting. Should we have a face to face working meeting there? We could work by email before.

Sent from my Windows Mobile phone

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Thursday, January 28, 2010 9:51 AM
To: 'wcarlo@peds.uab.edu' <wcarlo@peds.uab.edu>; 'nfiner@ucsd.edu' <nfiner@ucsd.edu>; 'adas@rti.org' <adas@rti.org>; 'mgantz@rti.org' <mgantz@rti.org>; 'wrich@ucsd.edu' <wrich@ucsd.edu>
Subject: Support

Would you like a call set up with the subcommittee prior to 2/15 for a discussion of the nejm responses?
Or do you prefer email? We could poll for a call and cancel it if it does not appear necessary

Rose

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Archer, Stephanie (NIH/NICHD) [E]
Subject: Re: SUPPORT | NEJM forms received
Date: Monday, February 01, 2010 5:02:50 PM

No
And some have submitted on-line

We can deal with these tomorrow

Thanks
Rose

From: Archer, Stephanie (NIH/NICHD) [E]
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Mon Feb 01 11:09:12 2010
Subject: SUPPORT | NEJM forms received

I gathered the NEJM forms from the fax machine, your chair, and the pile next to your printer.
Any other places I should look for these?

Here's what I have so far (yellow highlight is where someone faxed only one of the required forms):

NEJM Forms received

	Copyright Transfer	ICMJE Disclosure
The SUPPORT Trial: Randomized Trial of Oxygen Saturation Targets in Extremely Premature Infants (09-11781)		
Abbot R. Laptook, MD	X	X
Abhik Das, PhD		
Anthony J. Piazza, MD		
Beena G. Sood, MD MS		
Bradley A. Yoder, MD		
Brenda B. Poindexter, MD MS		
Brenda H. Morris, MD		
C. Michael Cotten, MD MHS	X	X
Dale L. Phelps, MD		
Edward F. Bell, MD		
Ivan D. Frantz III, MD		
Krisa P. Van Meurs, MD	X	
Kristi L. Watterberg, MD		X
Kurt Schibler, MD	X	X
Marie Gantz, PhD		
Michele C. Walsh, MD MS		
Nancy S. Newman, RN	X	X
Neil N. Finer, MD		
Nirupama Laroia, MD		
Pablo J. Sánchez, MD		

Richard A. Ehrenkranz, MD	X	X
Roger G. Faix, MD		
Rosemary D. Higgins, MD		
Shahnaz Duara, MD	X	X
T. Michael O'Shea, MD, MPH		
Vivek Narendran, MD MRCP	X	X
W. Kenneth Poole, PhD		
Wade Rich, RRT		
Waldemar A. Carlo, MD	X	X
Early CPAP versus Surfactant in Very Preterm Infants: The SUPPORT Trial (09-11783)		
Abbot R. Laptook, MD	X	X
Abhik Das, PhD		
Beena Sood, MD, MS		
Bradley A. Yoder, MD		
Brenda B. Poindexter, MD MS		
Brenda H. Morris, MD		
C. Michael Cotten, MD MHS	X	X
Edward Donovan		
Edward F. Bell, MD		
Ivan D. Frantz III, MD		
Krisa P, Van Meurs, MD	X	
Kristi L. Watterberg, MD		X
Kurt Schibler		
Marie Gantz, PhD		
Michele C. Walsh, MD MS		
Namasivayam Ambalavanan, MD		X
Nancy Newman, RN	X	X
Neil N. Finer, MD		
Nirupama Laroia, MD		
Pablo J. Sánchez, MD		
Roger G. Faix, MD		
Rosemary D. Higgins, MD		
Shahnaz Duara, MD	X	X
Susie Buchter, MD	X	X
T. Michael O'Shea, MD, MPH		
Vineet Bhandari, MD, DM	X	X
W. Kenneth Poole, PhD		
Wade Rich, RRT, CCRC		
Waldemar A. Carlo, MD	X	X

Higgins, Rosemary (NIH/NICHD) [E]

From: Rich, Wade <wrich@ucsd.edu>
Sent: Monday, February 01, 2010 11:01 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Finer, Neil; Gantz, Marie
Subject: Antenatal Paper

Follow Up Flag: Follow up
Flag Status: Completed

Hi Rose,

At the request of the reviewers, I would like to include the budgeted time for consent for SUPPORT in my paper and compare it to the time it actually took. Would that have been broken out on a budget somewhere ?

Wade

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Sunday, January 31, 2010 11:10 PM
To: Wally Carlo, M.D.; Higgins, Rosemary (NIH/NICHD) [E]; adas@rti.org; mgantz@rti.org; Rich, Wade
Cc: Cunningham, Meg
Subject: RE: Support

I am having trouble getting these forms. I will try at work –I am very happy to have Wally submit all the disclosure forms we need

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Sunday, January 31, 2010 3:05 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Finer, Neil; adas@rti.org; mgantz@rti.org; Rich, Wade
Cc: Cunningham, Meg
Subject: RE: Support

We need the disclosure forms of each author so we can do the one that goes in the paper. I checked the instructions on the web and can do the first draft (for both papers) once I get all forms or someone else can do it for both papers.

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Thu 1/28/2010 12:41 PM
To: Wally Carlo, M.D.; nfiner@ucsd.edu; adas@rti.org; mgantz@rti.org; wrich@ucsd.edu
Cc: Cunningham, Meg
Subject: RE: Support

Neil is not attending (though this would be great if he could attend. We could see if there is any time - Meg - can you look at the agenda and see if there is a time possible for SUPPORT Subcommittee?? Perhaps before the dinner on 2/11?

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Wally Carlo, M.D. [mailto:WCarlo@peds.uab.edu]
Sent: Thursday, January 28, 2010 1:39 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; wcarlo@peds.uab.edu; nfiner@ucsd.edu; adas@rti.org; mgantz@rti.org; wrich@ucsd.edu
Subject: RE: Support

We will be at the NRN meeting. Should we have a face to face working meeting there? We could work by email before.

Sent from my Windows Mobile phone

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] <higginsr@mail.nih.gov>
Sent: Thursday, January 28, 2010 9:51 AM
To: 'wcarlo@peds.uab.edu' <wcarlo@peds.uab.edu>; 'nfiner@ucsd.edu' <nfiner@ucsd.edu>; 'adas@rti.org' <adas@rti.org>; 'mgantz@rti.org' <mgantz@rti.org>; 'wich@ucsd.edu' <wich@ucsd.edu>
Subject: Support

Would you like a call set up with the subcommittee prior to 2/15 for a discussion of the nejm responses? Or do you prefer email? We could poll for a call and cancel it if it does not appear necessary

Rose

From: [Gantz, Marie](#)
To: [Das, Abhik](#); [Finer, Neil](#); [Wally Carlo, M.D.](#); [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Subject: RE: SUPPORT CPAP paper response
Date: Friday, January 29, 2010 8:39:55 PM

I am working on the requests and will get back to you next week as soon as I can. Note that I will be traveling for another project Mon-Wed.

Thanks,
Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Das, Abhik
Sent: Friday, January 29, 2010 10:50 AM
To: [Finer, Neil](#); [Wally Carlo, M.D.](#); [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Cc: Gantz, Marie
Subject: SUPPORT CPAP paper response

Attached please find my suggested changes appended to the revisions from Rose. The statistical responses incorporate some input I got from Ken. Marie can add stuff in as well. Please let me know whether you think the NEJM will find these adequate.

Thanks

Abhik

Abhik Das, PhD
Senior Research Statistician
Statistics and Epidemiology Unit
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20852

Phone: (301) 770-8214
e-mail: adas@rti.org

From: [Cunningham, Meg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Cc: [nfiner@ucsd.edu](#); [fmartinez@ucsd.edu](#); [Das, Abhik](#); [Gantz, Marie](#)
Subject: RE: SUPPORT MEETING
Date: Friday, January 29, 2010 12:07:13 PM

The call in number will be the same.

Within the USA
866-675-3256
Then, enter Participant Passcode:
560152 #

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, January 29, 2010 11:56 AM
To: Cunningham, Meg
Subject: FW: SUPPORT MEETING

From: Finer, Neil [<mailto:nfiner@ucsd.edu>]
Sent: Friday, January 29, 2010 11:50 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Martinez, Fernando
Subject: RE: SUPPORT MEETING

This will be fine Rose
Be well
Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Friday, January 29, 2010 8:26 AM
To: Finer, Neil; Martinez, Fernando
Cc: Boswell, Brittany; Cunningham, Meg
Subject: SUPPORT MEETING

Neil –
I spoke to Brittney in your office. We can have the SUPPORT SUBCOMMITTEE meet at the upcoming Steering Committee meeting at 1:15 PM ET (10:15 AM PT) . Let us know if this can work for you

Thanks

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
Pregnancy and Perinatology Branch
Center for Developmental Biology and Perinatal Medicine
Eunice Kennedy Shriver National Institute of Child Health and Human Development
National Institutes of Health

6100 Executive Blvd., Room 4B03
MSC 7510
Bethesda, MD 20892
For overnight delivery use Rockville, MD 20852
301-496-5575
301-496-3790 (FAX)
higginsr@mail.nih.gov

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "David A Randolph"; "wcarlo@peds.uab.edu"
Subject: RE: 2010 PAS Abstract Notification (#751628)
Date: Friday, January 29, 2010 8:45:00 AM

So sorry to hear this - thanks for the effort!
Rose

-----Original Message-----

From: David A Randolph [mailto:drdrdr@uab.edu]
Sent: Friday, January 29, 2010 12:56 AM
To: Higgins, Rosemary (NIH/NICHD) [E]; wcarlo@peds.uab.edu
Subject: FW: 2010 PAS Abstract Notification (#751628)

Wally and Rose,

Unfortunately the abstract was not accepted for presentation at PAS.

Regards, David

David A. Randolph, MD, PhD
Assistant Professor of Pediatrics
Division of Neonatology
University of Alabama in Birmingham
845 19th Street South, BBRB 834
Birmingham, AL 35205
(205) 996-9349 or (205) 934-4680

From: PAS - Marathon Multimedia [info@pas-meeting.org]
Sent: Thursday, January 28, 2010 4:33 PM
To: David A Randolph
Cc: campaign@marathonmultimedia.com
Subject: 2010 PAS Abstract Notification (#751628)

RE: Perinatal Acidosis and Outcomes in Extremely Low Birth Weight Infants (Abstract #: 751628)

Dear Dr. David Randolph:

We regret to inform you that, after careful review by a panel of experts in the field, your abstract entitled, "Perinatal Acidosis and Outcomes in Extremely Low Birth Weight Infants," whose presenting author is D.A. Randolph, has not been accepted for presentation at the 2010 Pediatric Academic Societies' Annual Meeting in Vancouver, BC, Canada. The program committee received a large number of abstract submissions, and the selection process is a difficult one for us.

Your abstract will be included in the official PAS Abstracts2View™, a CD and online product that allows users to search and access all abstracts submitted to the 2010 PAS Annual Meeting. Your abstract has been assigned publication number 660.

For your official disposition letter, please go to the following website. You will not receive this information via mail.

Website: <http://www.call4abstracts.com/pas>
Username: drdrdr

Password: @lashawn0513

We hope that you will continue your research efforts and look forward to seeing abstract submissions from you next November.

Thank you for your submission and support of the Pediatric Academic Societies.

If you have any questions, please feel free to contact Marathon Multimedia Technical Support at 507-333-1000, support@marathonmultimedia.com.

Sincerely,
The Pediatric Academic Societies

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "mcunningham@rti.org"
Subject: Re: Support
Date: Thursday, January 28, 2010 2:19:11 PM

Yes

I just sent an email to those involved

----- Original Message -----

From: Cunningham, Meg <mcunningham@rti.org>
To: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Thu Jan 28 14:13:14 2010
Subject: RE: Support

DO you mean, we are finding out today who was accepted?

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Thursday, January 28, 2010 2:01 PM
To: Cunningham, Meg
Subject: RE: Support

Overlap is likely best as long as neil can join -

can you send me the list of PAS submitted abstracts?? Today is the notification day and I want to remind the submitters. I don't have access to it right now.

Thasnk

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network

-----Original Message-----

From: Cunningham, Meg [<mailto:mcunningham@rti.org>]
Sent: Thursday, January 28, 2010 1:49 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.; nfiner@ucsd.edu; Das, Abhik; Gantz, Marie; wrich@ucsd.edu
Subject: RE: Support

I could overlap them with the NEST subcommittee, the only member that is on both is Michele Walsh and she is not attending the meeting. This would be at 1:15pm ET. The only other thing is to meet from 5-6 and push back dinner.

-----Original Message-----

From: Higgins, Rosemary (NIH/NICHD) [E] [<mailto:higginsr@mail.nih.gov>]
Sent: Thursday, January 28, 2010 1:41 PM
To: 'Wally Carlo, M.D.'; nfiner@ucsd.edu; Das, Abhik; Gantz, Marie; wrich@ucsd.edu
Cc: Cunningham, Meg
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Subject: Support

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Or do you prefer email? We could poll for a call and cancel it if it does not appear necessary

Rose

From: [Cunningham, Meg](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: Concept?
Date: Thursday, January 28, 2010 9:19:25 AM

Is this still being presented at the meeting?

Tentative Concept: Impact of initiating the SUPPORT trial on management and outcome of age-matched non-participants – Dr. Brion

Meg Cunningham
RTI International
701 13th St. NW, Ste. 750
Washington, DC 20005
tel: 202-974-7837
fax: 202-728-2095
www.rti.org

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Michele.Walsh@UHhospitals.org"
Subject: Re: Disclosures for SUPPORT
Date: Tuesday, January 26, 2010 5:37:33 PM

I sent them - let me know if you didn't get em!

From: Walsh, Michele <Michele.Walsh@UHhospitals.org>
To: Wally Carlo, M.D. <WCarlo@peds.uab.edu>; Neil_Finer <nfiner@ucsd.edu>
Cc: Higgins, Rosemary (NIH/NICHD) [E]
Sent: Tue Jan 26 17:24:00 2010
Subject: Disclosures for SUPPORT

Congrats to both of you for excellent work:
Cant wait to read the reviews!

Michele Walsh

Medical Director NICU
Co-Chief: Division of Neonatology
Rainbow Babies & Childrens Hospital
UH Case Medical Center
Professor, Department of Pediatrics
Case Western Reserve University
phone: 216-844-3759
FAX: 216-844-3380
michele.walsh@cwru.edu
michele.walsh@UHhospitals.org (emails are interchangeable)

Visit us at www.UHhospitals.org.

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From: [Walsh, Michele](#)
To: [Wally Carlo, M.D.](#); [Neil Finer](#)
Cc: [Higgins, Rosemary \(NIH/NICHD\)](#) [E]
Subject: Disclosures for SUPPORT
Date: Tuesday, January 26, 2010 5:24:54 PM
Attachments: [ICMJE-Disclosure-Form-102309.pdf](#)

Congrats to both of you for excellent work:
Cant wait to read the reviews!

Michele Walsh

Medical Director NICU
Co-Chief: Division of Neonatology
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ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

INSTRUCTIONS:

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form has five parts.

1. Identifying information.

Each author should submit a separate form. Provide complete information and double-check the manuscript number. If you are NOT the corresponding author please insert his or her name.

2. The work under consideration for publication.

Please provide information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The idea is to provide for the reader information about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. If you check the "No" box it means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds to pay you. If you or your institution did receive funds from a third party to support the work, check "Yes" along with the appropriate boxes to indicate the type of support and whether you or your institution received it.

3. Relevant financial activities outside the submitted work.

Please report all sources of revenue relevant to the submitted work that accrued either directly to you or were paid to your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. If there is any question, it is usually better to disclose a relationship than not to do so. Please note that your interactions with the work's sponsor outside the submitted work should be listed here. For each category list each entity on a separate line. Use as many lines as necessary to provide complete information. In addition, please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

The goal of this section is to provide information for our reviewers and readers about your interactions with entities in the biomedical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer. For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to benefit financially from the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as the NIH or the MRC, need not be disclosed. For example, if the NIH sponsored a piece of work you have been involved in but drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Financial relationships involving your spouse or partner or your children (under 18 years of age).

If monies from the types of relationships listed in Section 3 were paid to your spouse or partner or dependent children, please list the type of activity and source of the money.

5. Nonfinancial associations.

Please report any personal, professional, political, institutional, religious, or other associations that a reasonable reader would want to know about in relation to the submitted work.



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 1. Identifying Information.

Given Name:
(or first)

Michele

Surname:
(or last)

Walsh

Effective Date:

26-January-2010

Format example: 07-August-2008

Are you the corresponding author? Yes No

Manuscript Title:

Manuscript Identifying Number (if you know it):

Section 2. Information about the support of the work under consideration for publication.

Did you or your institution at any time receive payment or support in kind for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

No

Yes, specify nature of compensation

If you have more than one relationship, click "Add +" to add a row. Click "Del x" to delete an extra row.

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	No	Yes	No	Yes			
Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Case Western REserve Univ		Del x
							Add +
Consulting fee or honorarium	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Support for travel to meetings for the study or otherwise	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Case Western Reserve Univ		Del x
							Add +
Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +
Payment for writing or reviewing the manuscript	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del x
							Add +



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Type	Money Paid to You*		Money to Your Institution		Name of Entity	Comments**	
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			
Support in kind such as writing, provision of medicines or equipment, or administrative support	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +
Other	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>			Del X
							Add +

**Use this section to provide any needed explanation

Section 3. Information about relevant financial relationships outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with any entities that have an interest related to the submitted work. Use one line for each entity; add as many lines as you need. Use the comments column to indicate any additional information that you think a reader or editor would want to know about the compensation. Report relationships that were present during the 36 months prior to submission. In addition please disclose relationships that fall outside the 36-month window that readers may want to know about and could reasonably criticize you for not disclosing (for example, long-term financial relationships that are now ended).

If you have more than one relationship, click "Add +" to add a row. Click "Del X" to delete an extra row.

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Board membership	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Consultancy	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Employment	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Expert testimony	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Gifts	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +
Grants/grants pending	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			Del X
						Add +



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Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your institution	Entity	Comments	
Honoraria	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Payment for manuscript preparation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Patents (planned, pending or issued)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Royalties	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Payment for development of educational presentations including service on speakers' bureaus	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Stock/stock options	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Travel/accommodations expenses covered or reimbursed	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +
Other (err on the side of full disclosure)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>			De X
						Ad +

Section 4. Information about financial relationships involving your spouse or partner or your children (under 18 years of age).

Do your children or your spouse or partner have financial relationships with entities that have an interest in the content of the submitted work?

- No other relationships/conditions/circumstances that present potential conflict of interest
- Yes, the following relationships/conditions/circumstances are present (explain below):



ICMJE Uniform Disclosure Form for Potential Conflicts of Interest

Section 5. Information about relevant nonfinancial associations.

Do you have any relevant nonfinancial associations or interests (personal, professional, political, institutional, religious, or other) that a reasonable reader would want to know about in relation to the submitted work?

- No relevant nonfinancial relationships/conditions/circumstances to report.
- Yes, the following relevant nonfinancial relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Save Form

Higgins, Rosemary (NIH/NICHD) [E]

From: Finer, Neil <nfiner@ucsd.edu>
Sent: Tuesday, January 26, 2010 5:23 PM
To: Higgins, Rosemary (NIH/NICHD) [E]; Wally Carlo, M.D.; 'Das, Abhik'
Subject: RE: SUPPORT

That's fine with me Rose

Wally and I will start preparing responses to each query and get the help we need and then once these are drafted send out for the Subcommittee.

Neil

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Tuesday, January 26, 2010 12:40 PM
To: Wally Carlo, M.D.; Finer, Neil; 'Das, Abhik'
Subject: SUPPORT

I think it would be ok if the reviews went to the subcommittee – the steering committee is aware of the good news – just told them on the phone – would you like to send the reviews or do you want me to do it?? I will also send a brief note to the authors of each paper.

Thanks
Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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higginsr@mail.nih.gov

From: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
To: [Spong, Catherine \(NIH/NICHD\) \[E\]](#)
Subject: Confidential
Date: Tuesday, January 26, 2010 2:02:00 PM

Cathy

AWSEOME news from NEJM for the SUPPORT Trial papers– they have asked us for revisions on both papers and are proposing to publish them back-to-back if we respond appropriately!!!

Thanks for your unending SUPPORT on this one!!

Rose

Rosemary D. Higgins, MD
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Subject: New England Journal of Medicine - 10-00843
Date: Friday, January 22, 2010 3:12:07 PM

Dear Dr. Carlo and co-authors,

Thank you for submitting your manuscript, "Cytokines and Neurodevelopmental Outcomes in Extremely Low Birth Weight Infants" to the New England Journal of Medicine.

Your manuscript has been forwarded to members of our editorial staff, who will make an initial evaluation and decide whether it merits further consideration. You will be notified of the decision as soon as possible.

Your manuscript ID is 10-00843.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at <http://mc05.manuscriptcentral.com/nejm> and edit your user information as appropriate. You may also view the status of your manuscript at any time by checking For Authors section of the site.

We are undertaking evaluation of your manuscript with the understanding that neither the substance of the article nor the figures or tables have been published or will be submitted for publication elsewhere during the period of review.

Please provide the editors with copies of other manuscripts by you or your coauthors addressing similar or related research questions that are in preparation or under consideration at other journals. This does not apply to abstracts published in connection with scientific meetings or to news reports based on presentations at such meetings.

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Please call us at 617-734-9800 if you have any questions.

Sincerely,

Jeffrey M. Drazen, M.D.
Editor-in-Chief
New England Journal of Medicine
Distinguished Parker B. Francis Professor of Medicine
Harvard Medical School

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From: Roy Heyne
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](mailto:Higgins.Rosemary@NIH/NICHD)
Subject: Re: SUPPORT FU
Date: Wednesday, January 20, 2010 6:35:48 PM

Thanks for the positive feedback.

>>> "Higgins, Rosemary (NIH/NICHD) [E]" <higginsr@mail.nih.gov> 1/20/2010 2:35 PM >>>
CONGRATULATIONS!

Your site has no current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

Rosemary D. Higgins, MD
Program Scientist for the Neonatal Research Network
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higginsr@mail.nih.gov

From: [Blaisdell, Carol \(NIH/NHLBI\) \[E\]](#)
To: [Higgins, Rosemary \(NIH/NICHD\) \[E\]](#)
Subject: any updates?
Date: Wednesday, January 20, 2010 5:34:01 PM

Dear Rose,

Is SUPPORT likely to have media coverage for anything breaking in the next few months?

Dorothy needs to know for our leadership.

Thanks, Carol

Carol J. Blaisdell, M.D.
Medical Officer
Lung Developmental Biology and
Pediatric Pulmonary Diseases
Division of Lung Diseases, NHLBI/NIH
(301) 435-0222 phone

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Roger Faix"; "Bradley Yoder"; "Karen Osborne RN"; "Anna Bodnar"; "Shawna Baker"; "J. Ross Milley"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Wednesday, January 20, 2010 3:42:00 PM

CONGRATULATIONS!

Your site has not current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

Rosemary D. Higgins, MD
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Kristi Watterberg"; "rohls@salud.unm.edu"; "Conra Lacy"; "Rebecca Montman"; "JaFuller@salud.unm.edu"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Wednesday, January 20, 2010 3:42:00 PM
Importance: High

CONGRATULATIONS!

Your site has no current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Abbot Laptook"; "Vohr, Betty"; "Hensman, Angelita"; "sventura@wihri.org"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Wednesday, January 20, 2010 3:36:00 PM
Importance: High

CONGRATULATIONS!

Your site has no current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Michele Walsh"; "drfrcmd@aol.com"; "Nancy Newman"; "Bonnie Siner"
Cc: "Gantz, Marie"
Subject: SUPPORT FU
Date: Wednesday, January 20, 2010 3:35:00 PM
Importance: High

CONGRATULATIONS!

Your site has no current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

Rosemary D. Higgins, MD
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Pablo.Sanchez@UTSouthwestern.edu"; "Roy.Heyne@utsouthwestern.edu"; "Lizette.Torres"; "Nancy.Miller";
"Diana.Vasil"
Cc: "Gantz,Marie"
Subject: SUPPORT FU
Date: Wednesday, January 20, 2010 3:35:00 PM
Importance: High

CONGRATULATIONS!

Your site has no current missing SUPPORT FU outcomes. Keep up the good work and thanks for the unending effort!!

Rose

Rosemary D. Higgins, MD
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Gantz, Marie"
Cc: "Das, Abhik"
Subject: RE: SUPPORT FU
Date: Wednesday, January 20, 2010 11:17:00 AM

No problem – I have been bugging people about other studies including 6-7 year hypothermia FU

From: Gantz, Marie [mailto:mgantz@rti.org]
Sent: Wednesday, January 20, 2010 11:16 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Das, Abhik
Subject: RE: SUPPORT FU

Yes, I will do that. I apologize that I have not sent the FU reminders to you – I was so focused on the primary outcomes!

Marie

Marie Gantz, Ph.D.
Research Statistician
RTI International
mgantz@rti.org
828-254-6255

From: Higgins, Rosemary (NIH/NICHD) [E] [mailto:higginsr@mail.nih.gov]
Sent: Wednesday, January 20, 2010 11:13 AM
To: Gantz, Marie
Cc: Das, Abhik
Subject: SUPPORT FU

Marie

Can you continue to send me (monthly) the list of SUPPORT FU missing outcomes and closed windows? Also, can you look at the lost to FU and determine if we can assign any of the infants?

Thanks
Rose

Rosemary D. Higgins, MD
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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Juliann DiFiore"; "Walsh, Michele"
Cc: "Finer, Neil"; "Julie DiFiore"; "Martin, Richard"
Subject: RE: SUPPORT Updates
Date: Tuesday, January 19, 2010 1:31:00 PM

Great
Thanks
Rose

From: Juliann DiFiore [mailto:juliann.difiore@case.edu]
Sent: Tuesday, January 19, 2010 1:17 PM
To: Walsh, Michele
Cc: Finer, Neil; Higgins, Rosemary (NIH/NICHD) [E]; Julie DiFiore; Martin, Richard
Subject: Re: SUPPORT Updates

I sent out the latest draft of the proposal on Friday. I am hoping we can have it finalized by later this week.

Regards,

Julie

On 1/19/2010 12:19 PM, Walsh, Michele wrote:
Hi Julie and Richard:
On the conference call today, there was a request for
The formal proposal to analyze the entire trial saturation profiles.
I know that your protocol was near final. Could you update the group
On the status? Thanks

Michele Walsh
beeper 30642
Ph 216 844 3759

From: Finer, Neil [mailto:nfiner@ucsd.edu]
Sent: Monday, January 18, 2010 7:07 PM
To: Finer, Neil; 'Higgins, Rosemary (NIH/NICHD) [E]'; 'Wally Carlo, M.D.'; 'Michele Walsh'; 'Bradley Yoder'; 'Roger Faix'; 'Abbot Laptook'; 'kurt.schibler@cchmc.org'; 'Das, Abhik'; 'Nancy Newman'; 'Gantz, Marie'; 'Poole, W. Kenneth'
Cc: 'Petrie, Carolyn'; 'Zaterka-Baxter, Kristin'; Rich, Wade
Subject: RE: SUPPORT Updates

Hi Everyone
We will have a brief meeting tomorrow morning at 11:30 ETime
We have no news from the NEJM about the manuscripts

Agenda

- Review current follow-up progress
- Review the ROP adjudication data
- Review the FiO2 and SpO2 analyses

Discuss Secondaries – MRI, Growth and Pulmonary

Discuss other papers from secondary hypotheses

New Items

Talk to you in the morning

Neil

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From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Duara, Shahnaz"
Cc: "Finer, Neil"; "Navarrete, Cristina"; "Gantz, Marie"; "Das, Abhik"
Subject: RE: Growth secondary/SUPPORT
Date: Friday, January 15, 2010 2:58:00 PM

Yes,

I have copied Marie and Abhik – RTI can determine who best to work on this. I believe you have done mock tables, right??

Thanks

Rose

From: Duara, Shahnaz [mailto:SDuara@med.miami.edu]
Sent: Friday, January 15, 2010 2:54 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: 'Finer, Neil'; Navarrete, Cristina
Subject: Growth secondary/SUPPORT

Hi Rose,

Now that the SUPPORT main MS has been submitted and the PAS frenzy is past, would it be appropriate to look at the Growth secondary data and evaluate for MS?

Shahnaz

Higgins, Rosemary (NIH/NICHD) [E]

From: Fuller, Martha <mgfuller@ucsd.edu>
Sent: Thursday, January 14, 2010 2:11 PM
To: Newman, Jamie; Rich, Wade; Vaucher, Yvonne
Cc: Zaterka-Baxter, Kristin; Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject: RE: Revised Bayley III form to use for the remainder of your SUPPORT pts at 18 mo

Thanks, will review the video and forms.
Martha

From: Newman, Jamie [mailto:newman@rti.org]
Sent: Wednesday, January 13, 2010 12:53 PM
To: Fuller, Martha; Rich, Wade; Vaucher, Yvonne
Cc: Zaterka-Baxter, Kristin; Higgins, Rosemary (NIH/NICHD) [E]; Auman, Jeanette O.
Subject: Revised Bayley III form to use for the remainder of your SUPPORT pts at 18 mo

Martha,
Attached is the updated Bayley III (SF09A form) for you to use with the remainder of your 18 month follow-up visits for your SUPPORT patients with changes highlighted in yellow. I am also including a PDF of a clean copy of this form which I will soon post to the NRN website under: Protocols – SUPPORT – Secondary Studies – 18 Month FU - Forms

Since you key your SUPPORT Follow-up data in the SUPPORT DMS, you will need to wait to key the SF09A form for when this update has been made to the SUPPORT DMS. We will let you know when this has been done.

Also attached is the revised SF10A form that includes the motor component items. This is the administrative form that you send to Dr. Rose Higgins to describe incomplete visits. Since this form is not keyed in the data entry system, no updates will need to be made to your DMS for this form. I will soon post a clean copy of this form to the NRN website at the location indicated above.

For your records, I am also attaching the technical memo that went out on October 20, 2009 that describes the addition of the Bayley III motor component to the 18 mo follow-up visit (which includes babies enrolled in a randomized trial with 18 mo follow-up such as SUPPORT). Please refer to the updated 18 month Follow-up Manual for additional information on administering the motor component and completing the revised Bayley III form which is located on the NRN website under: Protocols/Follow Up/18 month/2010/Manual.

I realize you will be making a tape to send to Gold Standard, Harriet Friedman, on Jan 22 to be re-certified on the Bayley exam including the motor component. I realize you have been doing the motor component for clinical purposes but you may find it helpful to review the DVD of the motor component that was sent out on Oct 20 (Fed Ex receipt confirmation included below).

Please let me know if you have any questions. We appreciate your hard work in completing the remainder of your SUPPORT 18 month follow-up visits.

Thanks, Jamie

Jamie E. Newman, PhD, MPH
Statistics and Epidemiology
RTI International
Telephone: (919) 485-5719
Fax: (919) 485-7762
newman@rti.org

From: TrackingUpdates@fedex.com [mailto:TrackingUpdates@fedex.com]
Sent: Wednesday, October 21, 2009 12:57 PM
To: Newman, Jamie
Subject: FedEx Shipment 796046691958 Delivered

This tracking update has been requested by:

Company Name: RTI International
Name: Jamie Newman
E-mail: newman@rti.org

Message: Bayley III Motor Component DVD is being sent to Martha Fuller.

Our records indicate that the following shipment has been delivered:

Reference: 0208838.012.051
Ship (P/U) date: Oct 20, 2009
Delivery date: Oct 21, 2009 9:55 AM
Sign for by: A.WILSON
Delivered to: Receptionist/Front Desk
Service type: FedEx Standard Overnight
Packaging type: FedEx Envelope
Number of pieces: 1
Weight: 0.50 lb.
Special handling/Services: Deliver Weekday

Tracking number: [796046691958](#)

Shipper Information

Shipper Information	Recipient Information
Jamie Newman	Martha Fuller
RTI International	200 W. Arbor Drive, 8774
3040 Cornwallis Rd	San Diego
Cox Bldg, Rm 330	CA
RTP	US
NC	92103
US	
27709	

Please do not respond to this message. This email was sent from an unattended mailbox. This report was generated at approximately 11:57 AM CDT on 10/21/2009.
[Learn more](#) about new ways to track with FedEx.

All weights are estimated.

To track the latest status of your shipment, click on the tracking number above, or visit us at fedex.com.
This tracking update has been sent to you by FedEx on the behalf of the Requestor noted above. FedEx does not validate the authenticity of the requestor and does not validate, guarantee or warrant the authenticity of the

request, the requestor's message, or the accuracy of this tracking update. For tracking results and fedex.com's terms of use, go to fedex.com.

Thank you for your business.

From: Higgins, Rosemary (NIH/NICHD) [E]
To: "Das, Abhik"
Subject: RE: SUPPORT papers
Date: Wednesday, January 13, 2010 10:49:00 AM

Hopefully they are doing their "re-write." Neil's paper was back "With the editor" on 12/17 and Wallys' was there on 12/31. if they didn't want them, I think we would have gotten a rejection by now. Keep your fingers crossed.

Rose

From: Das, Abhik [mailto:adas@rti.org]
Sent: Wednesday, January 13, 2010 10:45 AM
To: Higgins, Rosemary (NIH/NICHD) [E]
Subject: SUPPORT papers

I am surprised that we still haven't heard from the NEJM yet. The suspense is killing me!

Abhik Das, Ph.D.
Senior Research Statistician
RTI International
6110 Executive Blvd., Suite 902
Rockville, MD 20852-3903
e-mail: adas@rti.org
Phone: 301-770-8214
Fax: 301-230-4646

From: Higgins, Rosemary (NIH/NICHD) [E]
To: Roger Faix
Cc: Karen Osborne RN; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: Progress report for non-competing renewal
Date: Wednesday, January 06, 2010 2:04:52 PM
Attachments: IRB Approval template[1].doc

Sorry about that. Here you go. Let us know if you need any more assistance with this.

Regards

Rose

Rosemary D. Higgins, MD

Program Scientist for the *Eunice Kennedy Shriver* NICHD Neonatal Research Network

Pregnancy and Perinatology Branch

CDBPM, NIH

6100 Executive Blvd., Room 4B03

MSC 7510

Bethesda, MD 20892

For overnight delivery use Rockville, MD 20592

301-435-7909

301-496-5575

301-496-3790 (FAX)

higginsr@mail.nih.gov

From: Roger Faix [Roger.Faix@hsc.utah.edu]
Sent: Wednesday, January 06, 2010 12:20 PM
To: Higgins, Rosemary (NIH/NICHD) [E]
Cc: Karen Osborne RN
Subject: RE: Progress report for non-competing renewal

Hi Rose!

The IRB template dose not appear to have been attached. Could you please send that again? Many thanks for your help!

Roger

From: Higgins, Rosemary (NIH/NICHD) [E] [higginsr@mail.nih.gov]
Sent: Wednesday, January 06, 2010 6:45 AM
To: Roger Faix
Cc: Karen Osborne RN; Poe, Grace (NIH/NICHD) [E]; Archer, Stephanie (NIH/NICHD) [E]
Subject: RE: Progress report for non-competing renewal

Roger

You will need to complete the PHS 2590 form – see requirements below. I have also attached the IRB template (you may use or develop your own) for reporting the dates for each NRN study. Let me know if you need more help. Also, the email may have also gone to your grants and contracts office, so they may be able to forward the request for the Type 5 non-competing application.

Rose

Reporting Requirements

NIH requires that grantees periodically submit reports. For all of the reports discussed in this section, grantees are reminded that they are due at specific times during the life cycle of a grant award. It is important that all reports are accurate, complete, and submitted on time.

Progress Reports

Progress reports are usually required annually as part of the non-competing continuation award process. The "Grant Progress Report" (PHS 2590) or equivalent documentation must be submitted to (and approved by) the NIH to non-competitively fund each additional budget period within a previously approved project period (competitive segment).

The information to be included in the progress report is specified in the PHS 2590 instructions, which also include alternate instructions for awards under Streamlined Non-competing Award Process (SNAP). Non-competing progress reports are submitted directly to NIH. Forms for non-competing grant progress reports are available at <http://grants.nih.gov/grants/funding/2590/2590.htm>.

If your award is eligible for the eSNAP, you may file an electronic progress report 45 days before the grant anniversary date. Non-SNAP awards should be submitted 60 days before the grant anniversary date.

Other factors related to your project might add additional requirements. For example, if you are working with human subjects, you need to get your certification of IRB approval re-approved every year of your award. Likewise, if you're working with research animals, you need to get your certification of IACUC approval re-approved every three years.

Invention Reports

Regulations require that grantee organizations report all inventions to the awarding agency (see NIH Grants Policy Statement), as well as include an acknowledgement of federal support in any patents. Grantee organizations are expected to use the Web-based Interagency Edison system (iEdison). NIH funding recipients are expected to use this system to comply with the Bayh-Dole Act (P.L. 96-517) and related intellectual property reporting requirements.

For more information on the policies that govern Invention Reporting, see the iEdison Web site.

From: Roger Faix [mailto:Roger.Faix@hsc.utah.edu]

Sent: Tuesday, January 05, 2010 5:06 PM

To: Higgins, Rosemary (NIH/NICHD) [E]

Cc: Karen Osborne RN

Subject: Progress report for non-competing renewal

Hi Rose!

I sustained an e-mail disaster recently and lost all of the e-mails from my in-box dated earlier than 12/30/09. This, unfortunately, included a notice from the NIH about the progress report and non-competing renewal. My ITS folks are working on recovering the e-mails, but (in the event that they are unsuccessful), could you help me get another copy of that communication so my colleagues and I can meet the February deadline?

Many thanks!

Roger

NRN IRB APPROVALS

<u>PROTOCOL NAME</u>	<u>PROTOCOL NUMBER</u>	<u>MOST RECENT DATE OF APPROVAL</u>	<u>APPROVED THROUGH</u>
Survey of Morbidity and Mortality Among Very Low Birth Weight Infants			
NICHD GDB Follow up of Very Low Birth Weight Infants			
A Randomized Trial of Aggressive or Conservative Phototherapy Treatment for Extremely Low birth Weight Infants			
Early Diagnosis of Nosocomial Candidiasis			
Neurodiagnostic Evaluations That Assist in the Prediction of Adverse Outcome Following Acute Perinatal Encephalopathy			

<u>PROTOCOL NAME</u>	<u>PROTOCOL NUMBER</u>	<u>MOST RECENT DATE OF APPROVAL</u>	<u>APPROVED THROUGH</u>
Association of Apolipoprotein E (Apo E) Genotype with Brain Injury and Neurodevelopmental Outcome in Infants with Hypoxic Ischemic Encephalopathy			
The Surfactant Positive Airway Pressure & Pulse Oximetry Trial in Extremely Low Birth Weight Infants (SUPPORT Study)			
Antenatal Screening & Consent in a Research Network Model (SUPPORT Study secondary)			
Neuroimaging and Neurodevelopmental Outcome: A Secondary Study to SUPPORT			
Breathing Outcomes (SUPPORT Study Secondary)			
Post-natal Growth of Infants Enrolled in the NICHD Neonatal Network Oxygen Saturation (SUPPORT) Study: A Proposed Secondary Study			
Extended follow-up at 6-7 years of age of patients enrolled in the Neuroimaging and Neurodevelopmental Outcome			

Secondary to SUPPORT			
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<u>PROTOCOL NAME</u>	<u>PROTOCOL NUMBER</u>	<u>MOST RECENT DATE OF APPROVAL</u>	<u>APPROVED THROUGH</u>
Long Term Follow Up of Children in the Randomized Controlled Trial of Induced Hypothermia for Hypoxic-Ischemic Encephalopathy			
Blood Inositol Status Among Neonates in 2005			
Single Dose Intravenous Inositol Pharmacokinetics in Preterm Infants			
Multiple Dose Intravenous Inositol Pharmacokinetics in Preterm Infants			
Early Onset Sepsis – An NICHD/CDC Surveillance Study			
PCV-7			
6-24 hour hypothermia			
Hypotension in term and late preterm infants: an observational study			
A Multi-center Randomized Trial of Laparotomy vs. Drainage as the Initial Surgical Therapy for ELBW Infants with Necrotizing Enterocolitis (NEC) or Isolated Intestinal Perforation (IP): Outcomes at 18-22 months Adjusted Age			

Early Blood Pressure Management in Extremely Preterm Infants			
Cerebral Function Monitoring and Brain Injury in Preterm Infants: Correlation with Neuroimaging Abnormalities and Neurodevelopmental Impairment- A Pilot Study			