Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING SUMMARY

September 9–10, 2021

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
***EUNICE KENNEDY SHRIVER* NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**
NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL
MEETING SUMMARY
September 9–10, 2021[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 177th meeting at 12:00 p.m. on Thursday, September 9, 2021, by National Institutes of Health (NIH) VideoCast. The meeting was open to the public on September 9 from 12:00 to 4:20 p.m. As provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463 for the review, discussion, and evaluation of grant applications and related information, the meeting was closed to the public on September 10, 2021, from 12:00 p.m. until 5:00 p.m.

Dr. Diana W. Bianchi, Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:
Diana W. Bianchi, M.D. (Chair)
Shari L. Barkin, M.D.
Susan Bookheimer, Ph.D.
Christina M. Bucci-Rechtweg, M.D.
Michele Caggana, Sc.D.
John P. Coughlin, M.D.
Kathleen B. Egan, Ph.D.
Lucky Jain, M.D.
Catherine E. Lang, Ph.D.
Missy Lavender, M.B.A.
Martin Matzuk, M.D., Ph.D.
Genevieve S. Neal-Perry, M.D., Ph.D.
Carmen L. Neuberger, J.D.
Adam C. Resnick, Ph.D.
David H. Rowitch, M.D., Ph.D.
Annette Sohn, M.D.
Alan Thenevet N. Tita, M.D., Ph.D., M.P.H.
Rebeca Wong, Ph.D.
Anthony J. Wynshaw-Boris, M.D., Ph.D.

National Advisory Board on Medical Rehabilitation Research Council liaison:
Arthur English, Ph.D.

Department of Defense:
COL (Ret.) Paul F. Pasquina, M.D. (absent)

***Ex officio* members:**
Patricia Dorn, Ph.D.
Aaron M. Lopata, M.D., M.P.P.

Executive Secretary:
Dennis Twombly, Ph.D.

[1] Members absent themselves from the meeting when the Council discusses applications from their own institutions or when a conflict of interest might occur. The procedure applies only to individual applications discussed, not to en bloc actions.

Others present:
Members of NICHD staff
Members of NIH staff
Members of the public

I. CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi welcomed members of the NACHHD Council and other participants to this meeting.

Review of Confidentiality and Conflicts of Interest

Dr. Twombly reminded Council members that all members were required to read, agree to, and sign the confidentiality and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. Before the meeting, Council members had received a conflict-of-interest certification form, which they were required to sign. Dr. Twombly also reminded Council members that they are required to recuse themselves and leave the virtual meeting before any discussion involving any organizations or universities for which they are in conflict, in addition to those listed in the Council Action document. Council members are not allowed to serve on the NIH peer review panel while serving as Council members, because NIH policy indicates that individuals may not serve on both the first and second levels of peer review.

Council Minutes

A motion to approve the June 7–8, 2021, NACHHD Council meeting minutes carried.

Future Meeting Dates

Dr. Twombly reviewed future Council meeting dates:

January 11–12, 2022 (virtual)
June 15, 2022 (6710B Rockledge Drive, Bethesda, Maryland)
September 13, 2022 (6710B Rockledge Drive, Bethesda, Maryland)

II. NICHD DIRECTOR'S REPORT

Dr. Bianchi delivered the director's report.

NIH Budget

The President's May 2021 budget request for fiscal year (FY) 2022 included a significant increase in funding for NIH and proposed moving two programs from the NIH Office of the Director to NICHD: the Environmental influences on Child Health Outcomes (ECHO) Program and the INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE (INCLUDE) Project. These moves would have increased the NICHD budget by $1.9 billion. The House of Representatives, however, did not include this proposal in its budget resolution, although the House budget does include $30 million for the Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone (IMPROVE) initiative and $15 million for research on SARS-CoV-2 in children. Proposed NIH funding increases include set-aside funds

for many initiatives that will affect NICHD work, including cybersecurity initiatives and the Gabriella Miller Kids First Research Program. The President's budget request also included $6.5 billion for NIH to establish the new Advanced Research Projects Agency for Health, but this amount was reduced to $3 billion in the House budget. NIH has led several listening sessions to discuss plans for this program.

The Senate has not marked up its budget resolution, so the federal government is unlikely to have an approved FY 2022 budget by the end of FY 2021 on September 30, 2021. Once the Senate does pass its budget resolutions, the two budgets must be reconciled and the President must sign the final budget.

COVID-19 Research Updates

Dr. Bianchi encouraged NACHHD Council members to check the COVID-19 research and NICHD website, which is updated regularly.

In the week of September 2, 2021, 251,781 U.S. children received positive COVID-19 test results, the highest number since the pandemic began. Children accounted for 14% of all COVID-19 cases in the United States earlier in the pandemic, but they now make up more than one-quarter of cases.

Whether the delta variant of SARS-CoV-2 results in more severe disease in children is difficult to determine. The number of COVID-19 cases and hospitalizations in children have risen dramatically, but the reason might be that the delta variant is more severe or that children younger than 12 years are not yet eligible for COVID-19 vaccination. Only 45% of adolescents have received both doses of a COVID-19 vaccine. Furthermore, an inverse relationship exists between the number of adults who are fully vaccinated in a community and the number of children with COVID-19 in that community.

Other COVID-19-related hot topics that NICHD is addressing include the effects of masking on SARS-CoV-2 transmission and child development, effects of parental vaccination on children, and how to safely return children to in-person schooling. NICHD is also tracking data on multisystem inflammatory syndrome in children (MIS-C). MIS-C case numbers spiked in early 2021 and then dropped steadily through July. As COVID-19 case numbers rise, the number of MIS-C cases is likely to increase again.

Examples of NIH and NICHD research on COVID-19 in children include the following:

- The Predicting Viral-Associated Inflammatory Disease Severity in Children with Laboratory Diagnostics and Artificial Intelligence (PreVAIL kIds) initiative, part of Rapid Acceleration of Diagnostics (RADx^{SM}) Radical (RADx-RAD), which is funding eight teams to identify risk factors for MIS-C, including potential biomarkers (NIH support), and ways in which to distinguish MIS-C from other diseases such as Kawasaki.
- Researching COVID to Enhance Recovery to study the post-acute sequelae of SARS-CoV-2 infection, including in pediatric and pregnant cohorts (NIH support)
- Studies of the impact of the COVID-19 pandemic on population fertility, roles of pandemic-related stress on fertility plans, and effects of maternal COVID-19 on birth outcomes (including differential effects in population subgroups) (NICHD support)

- One-year supplemental grants to five institutions to study links between COVID-19 vaccination and menstrual changes (NICHD support)

NIH recently convened a panel that recommended standardized criteria for defining infection of the placenta with SARS-CoV-2 using techniques that allow viral detection and localization in placental tissue.

Maternal Morbidity and Mortality

Dr. Bianchi and other NIH leaders, including NIH Director Francis Collins, M.D., Ph.D., met with members of the Black Maternal Health Caucus on July 20 to discuss ways to reduce health disparities in maternal mortality.

New NIH activities related to maternal morbidity and mortality include the following:

- Creation of a new NIH-wide reporting category for maternal morbidity and mortality research
- NICHD's participation in the White House Interagency Policy Committee on Maternal Health
- IMPROVE supplements for research on the intersection among maternal health, structural racism, and discrimination and the effects of the COVID-19 pandemic
- NICHD's Decoding Maternal Morbidity Data Challenge, an effort to develop new ways of analyzing data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be to identify predictors of maternal morbidity
- Research to reduce or eliminate maternal morbidity and mortality caused by infections and sepsis

STrategies to enRich Inclusion and achieVe Equity (STRIVE) Initiative

STRIVE is hosting workshops on various topics, including the effect of social identity on health and community-based research strategies to mitigate health disparities in NICHD populations. All of these workshops are or will be available on the NIH VideoCast website.

NICHD Staff Updates

Dr. Bianchi announced the appointment of Chris McBain, Ph.D., as acting scientific director at NICHD. New NICHD staff include the following:

- Rebecca Rosen, Ph.D., director, Office of Data Science and Sharing
- Helena Ahn, Ph.D., program officer, Gynecologic Health and Disease Branch, Division of Extramural Research
- Teri Pailen, team lead, Grants Management

NICHD recently welcomed one new presidential management fellow, Emma Carpenter, Ph.D., and two new AAAS fellows, Dave Gutekunst, Ph.D., and Karen Mulak, Ph.D. NICHD is conducting a second search for a permanent scientific director after the candidate selected from the first search was unable to relocate to assume the position. NICHD is also conducting searches for other positions, including tenure-track investigators in basic and translational science. Information on all open positions is available at Jobs at NICHD.

Discussion

Dr. Coughlin asked about risk factors for MIS-C. Dr. Bianchi replied that risk factors for death in children with MIS-C appear to be Black or Hispanic race and ethnicity, male sex, and obesity.

Dr. Sohn asked whether more NICHD experts are likely to be featured in media stories, especially about the safe return to in-person schooling and vaccinations for adolescents and children. Dr. Bianchi explained that the main NIH spokespersons on COVID-19 are Anthony Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases, and Dr. Collins. NICHD does provide information to the NIH Office of the Director on issues in which it has expertise upon request.

Dr. Neal-Perry asked about racial disparities in breakthrough infections in adults who have received both COVID-19 vaccine doses and whether obesity is a risk factor for such infections. Dr. Bianchi said that obesity is a risk factor for breakthrough infections in adults. However, she was unaware of data on racial disparities in breakthrough infections in adults or children.

Dr. Tita asked about new initiatives to address maternal mortality. Dr. Bianchi explained that NICHD informed the Black Maternal Health Caucus that building programs to address this issue would require sustainable funding.

Dr. Bookheimer asked about research on disparities in COVID-19 severity among children with intellectual and developmental disabilities (IDD). Dr. Bianchi explained that the Return-to-School initiative that would be discussed later in this meeting includes several programs for children with IDD.

Dr. Egan asked whether fertility studies are assessing the effects of COVID-19 vaccines on male fertility in addition to female fertility. Dr. Bianchi said that no such effects have been reported to date, but NICHD has opportunities to address this question. Dr. Neal-Perry pointed out that the vaccines have not affected fertility in women. Dr. Bianchi agreed that no evidence to date indicates that vaccines affect fertility in women, although social media reports have spread misinformation on this topic.

III. ANNUAL DIVISION OF INTRAMURAL RESEARCH REPORT

Chris J. McBain, Ph.D., acting scientific director, NICHD, summarized his education and experience. His primary interest beyond research is mentoring students, postdoctoral fellows, and early-stage investigators (ESIs). He encourages his fellows to apply for external funding to gain experience writing grant applications. Dr. McBain also works with many NIH partnership programs for graduate students to spend time at NIH.

Overview of NICHD's Intramural Research Program

The NICHD Intramural Research Program has two divisions: the Division of Intramural Research (DIR), which conducts basic, clinical, and translational research, and the Division of Intramural Population Health Research (DIPHR). The DIR has approximately 830 employees, including 60 principal investigators (PIs), 59 staff scientists, and 297 trainees. PIs in the division

may join 12 scientifically based affinity groups. A mentoring committee helps junior PIs navigate the pitfalls of setting up a research program and earning tenure.

The DIR's budget is $207,056,000, or 14% of the NICHD budget. Between FY 2018 and FY 2021, the number of DIR personnel dropped as the cost of research rose, and the division's staff declines by approximately 2% to 5% each year. NICHD has approximately 300 intramural trainees each year. Half are postdoctoral fellows, and the rest are recent college graduates, graduate students, clinical fellows, and summer students.

Recent new hires include the following:

- Laverne Mensah, M.D., NICHD's first deputy clinical director
- Katherine Rogers, Ph.D., a tenure-track investigator
- Sarah Sheppard, M.D., Ph.D., a tenure-track investigator and the DIR's first participant in the NIH Distinguished Scholars Program
- Two new assistant clinical investigators, An Dang Do, M.D., and Christina Tatsi, M.D.
- Two new tenure-track DIPHR investigators, Bobby Cheon, Ph.D., and James Morton, Ph.D.

NICHD is recruiting a new DIPHR director. Una Grewal, Ph.D., M.P.H., is serving as interim director until the permanent director is hired.

Recent honors and awards for DIR investigators include the following:

- Election of Joan Marini, M.D., Ph.D., to the Association of American Physicians
- 2021 Eduard Rhein Stiftung Technology Award from the Eduard Rhein Foundation of Germany to Peter Basser, Ph.D.
- Endocrine Society's Outstanding Clinical Investigator Award and election to the Czech Medical Academy for Karel Pacak, M.D., D.Sc., Ph.D.

Education Updates

Key activities of the DIR Office of Education include the following:

- Public speaking and teaching: job talks, individual coaching, elevator speeches, syllabus and curriculum development with the University of Maryland, and graduate student talks during monthly PI meetings
- Grantsmanship and publishing: an annual grants workshop, guidance for NIH applications, mock study section workshops, and a 3-week grant writing course
- Careers: job interview preparation, networking, editing of job application materials, individualized guidance with annual reviews, exploration sessions for various career paths, and preparations for industry success
- Virtual programming: virtual platforms for one-on-one advising and career counseling and for all professional development programming and grants submissions

NICHD intramural diversity initiatives support the DIR commitment to recruit, train, support, and sustain a diverse group of talented young scientists, including those from groups that are traditionally underrepresented in science. These initiatives are as follows:

- The NICHD Developing Talent Scholars Program, for postbaccalaureate fellows and graduate students
- The Fellows Recruitment Incentive Award, for postdoctoral fellows
- The summer trainee program
- The Biology Secondary Honors Program and Career Planning and Professional Development Seminar Series, in partnership with Howard University's College of Arts and Sciences

Competitive Awards for DIR PIs and Trainees

Competitive award opportunities for DIR investigators and trainees include those listed below:

- Opportunities for Collaborative Research at the NIH Clinical Center (U01) to support studies conducted, at least in part, at the NIH Clinical Center and led by one extramural and one intramural PI
- The Office of AIDS Research Innovation Fund, which provides a year of funding for high-priority HIV/AIDS research
    - NICHD had three awardees in 2021.
- The NIH Center on Compulsive Behaviors Fellowship, for postdoctoral fellows interested in studying topics aligned with the center's mission
    - NICHD had four awardees in 2021.
- NICHD scientific director's awards, which provide 2 years of funding for collaborative research and supported 11 research projects in FY 2020–21
- NICHD Young Investigator Awards, a new program in FY 2021 aimed at promoting the research careers of intramural ESIs that has issued 22 basic science, clinical, and epidemiology research awards

Discussion

Dr. Bookheimer said that the DIR accomplishments described by Dr. McBain are extraordinary, and she was particularly pleased with the transition from a hierarchical structure to a flatter structure. This transition should be a model for all of the NIH institutes and centers (ICs).

Dr. Wynshaw-Boris asked whether DIR trainees have received NIH Pathway to Independence (K99/R00) awards. Dr. McBain explained that the DIR encourages its postdoctoral fellows and trainees to apply for a variety of funding opportunities, including the Pathway to Independence program. NICHD holds workshops twice a year to introduce postdoctoral fellows to NIH funding opportunities and information on how to plan for the next phase of their careers. NIH trainees have received several K99/R00 awards.

Dr. Jain asked about the target ratio between intramural and extramural funding. Dr. Bianchi replied that Congress expects each NIH IC to devote approximately 10% to 12% of its budget to intramural research, and only five ICs devote a higher proportion than NICHD.

Dr. Jain asked whether recipients of the NICHD Young Investigator Awards can be placed at NICHD-funded extramural laboratories. Dr. Bianchi explained that this program is modeled on a similar program at Tufts University that supports the careers of young women scientists, but NICHD's program is not limited to women. Criteria for the award include the candidate's career

potential and the scientific merit of their proposed research. These are small grants, but Tufts found that recipients continue their scientific careers and obtain extramural funding.

Dr. Wong asked whether the DIR provides training for mentors who guide young scholars from underrepresented communities. Dr. McBain recently met with Marie A. Bernard, M.D., the chief officer for scientific workforce diversity at NIH, and one of the issues they discussed was mentorship for students and ESIs from underrepresented communities. An NIH initiative will recruit mid-career mentors through the Distinguished Scholars Program, and Dr. McBain is encouraging NICHD to do the same. Another DIR program is assigning a coaching mentor to young tenure-track investigators to help them develop mentoring skills.

Dr. Rowitch approved of the DIR's focus on young scientists and team science. Dr. Neal-Perry suggested that Dr. McBain and other DIR leaders write a white paper or journal article discussing the lessons learned from their successful programs.

IV. SCIENTIFIC PRESENTATION: FERTILITY PRESERVATION IN CHILDREN AT RISK OF GONADAL DYSFUNCTION

Veronica Gomez-Lobo, M.D., director, Pediatric and Adolescent Gynecology, NICHD, explained that at birth, female infants have a set number of follicles, and this number decreases over the lifetime. Two techniques for preserving female gametes are oocyte cryopreservation and the newer technique of ovarian tissue cryopreservation (OTC).

OTC is the only fertility preservation option for prepubertal children at risk of gonadal dysfunction and, for those with cancer, does not require delays in cancer treatment. In this procedure, an ovary or ovarian tissue is removed laparoscopically and is transplanted back into the patient when she is ready to have children. The procedure has resulted in approximately 200 live births but only 1 live birth resulting from tissue collected before puberty. The live birth rate, at 23% to 41%, is lower than the 51% live birth rate after natural conception. The benefits of OTC in special populations have not been studied.

Noncancerous indications for OTC include those described below:

- Girls with *Turner syndrome* have one normal X chromosome and one missing or altered sex chromosome. Approximately 33% to 50% enter puberty spontaneously, 14% to 20% have spontaneous menarche, and 5% have a spontaneous pregnancy.
- *Classic galactosemia* is a rare inborn error of galactose metabolism that can result in neurodevelopmental impairment and, in 80% of women and girls with the condition, primary ovarian insufficiency. Approximately half of girls with classic galactosemia have spontaneous menarche, and approximately half of them can conceive spontaneously.
- Many girls and women with *premature ovarian insufficiency* not related to cancer therapy have ovarian function, but it is intermittent and unpredictable. Approximately 5% to 10% of women with this condition conceive spontaneously.

If girls with these conditions reach puberty and menstruate, they can preserve their fertility with OTC or oocyte cryopreservation. However, these conditions are associated with accelerated or

early follicle loss. The question is thus whether cryopreservation can allow these girls to take action before follicle loss and thaw the functioning tissue when they are ready to have children.

An NICHD intramural research project will offer OTC to prepubertal girls with Turner syndrome or classic galactosemia and to adolescents with recent premature ovarian insufficiency. Of the gonadal tissue collected, 80% will be stored for the patient and 20% will be stored for research. This study will determine whether participants have ovaries containing viable follicles. The study will also use single-cell and single-nucleus RNA sequencing to explore the mechanisms of follicle loss in these patients.

In addition to the above study, the Pediatric and Adolescent Gynecology Program is working to define the "normal" regarding ovarian tissue in young populations. Much of the research on fertility preservation in children at risk of gonadal dysfunction was conducted by the Oncofertility Consortium. NICHD is collecting images of ovarian tissue collected during OTC in the NICHD/Oncofertility Tissue Image Database to help understand normal ovarian tissue biology. In collaboration with the National Cancer Institute (NCI) Artificial Intelligence Core, NICHD investigators will develop methods for automated counting and classification of follicles and machine learning techniques to evaluate differences in tissues. In addition, ovarian anatomy nomenclature workshops have brought together experts to establish a rigorously defined, reproducible ovarian anatomy nomenclature.

Knowledge gaps in the field of fertility and fertility preservation in these populations are as follows:

- Can OTC arrest follicle loss?
- What is the quality of follicles and stroma in ovarian cortical tissue?
- What is the mechanism of ovarian dysfunction and follicle loss?
- What options are available for prevention?
- What is the optimal age for OTC?
- Does removing an ovary laparoscopically further decrease the ovarian follicle pool?
- Is follicle loss after transplantation greater in people with these conditions?

Discussion

Susan Taymans McClure, Ph.D., a program director in NICHD's Fertility and Infertility Branch, asked about the number of pregnancies attempted with cryopreserved ovarian tissue collected from prepubertal girls. Dr. Gomez-Lobo replied that very few such pregnancies have been attempted. Of more than 500 OTCs conducted by the Oncofertility Consortium, only two resulted in tissue transplants. This research is challenging, because obtaining answers takes decades.

Dr. Wynshaw-Boris asked about research to find the causes of gonadal dysfunction in girls and women with the three conditions. Dr. Gomez-Lobo replied that researchers are using whole exome sequencing to identify candidate genes. The pathways to gonadal dysfunction differ in patients with each of the three conditions, and not enough research has been conducted, particularly in girls with premature ovarian insufficiency.

Dr. Resnick suggested that NICHD integrate data from intramural and extramural research programs, especially for studies of rare diseases. Dr. Gomez-Lobo explained that the nomenclature workshops included representatives of the Human Cell Atlas and the Human BioMolecular Atlas Program, which will integrate the resulting nomenclature, and many opportunities are available to share data. Furthermore, the research she had described could not be done extramurally, because it could only be done at the NIH Clinical Center.

Dr. Jain asked whether NICHD could support a central data registry to track long-term outcomes of patients who undergo cryopreservation. Dr. Gomez-Lobo replied that data from the NICHD study will be available to the research community, and all of the data will be stored in a central database.

V. VOICE OF THE PARTICIPANT: IMPACT OF TURNER SYNDROME AND PREMATURE OVARIAN INSUFFICIENCY ON CHILDREN AND FAMILIES

Kelly Ranallo, founder and president, Turner Syndrome Global Alliance (TSGA), has a daughter, Allie, who has Turner syndrome. Allie recently graduated from college and is now working on biologic agent development for rare diseases.

Although Turner syndrome was first identified several decades ago, many gaps remain in understanding its effects. Many studies have shown the impact of infertility on quality of life, mental health, and long-term relationships throughout the lifespan.

When Allie's younger sister was born, Allie pretended to be pregnant and talked constantly about becoming a mother and what would happen when she had babies. At that time, Ms. Ranallo and her daughter did not know that Allie's medical condition would change her family planning journey.

When Allie was 8, she received her Turner syndrome diagnosis. Like many patients with rare genetic conditions, Allie's mosaic Turner syndrome was not identified at birth, and her diagnostic journey took almost a decade. Once Allie's diagnosis was confirmed, her mother was devastated by the knowledge that her daughter might never be able to have her own biological children.

Allie underwent spontaneous puberty but had an adverse reaction to hormone replacement therapy and was referred to the adolescent gynecology department. A specialist there determined that Allie did not require hormone replacement therapy at that time but might benefit from a discussion about fertility preservation. If Allie had not had an adverse reaction to hormone replacement therapy, she might never have started on the fertility preservation pathway.

Allie decided, with help from her family, to undergo oocyte cryopreservation at the age of 17. This procedure is not easy and has psychological, physical, and financial components. The team performing the procedure was excited because Allie had 26 follicles. However, after the procedure, the team informed Allie and her family that they could retrieve only six eggs. This unexpected outcome was extremely difficult due to the expectation that had been set. Hindsight,

if Allie and her family had known that the procedure might not result in any eggs, they would then have been pleased that six were harvested. Another challenge was the insurance company's denial of coverage of the cost to store Allie's frozen eggs. The company claimed that the procedure was experimental and did not have the necessary supportive research similar to the oncofertility population. Allie's parents therefore pay out of pocket to store the frozen eggs.

A 2014 survey completed by the TSGA found that only a small minority of parents of girls and women with Turner syndrome receive recommendations from a health care provider about discussing infertility with their daughters. In follow-up to the survey, health care providers stated that they do not have enough evidence to provide such guidance.

Ms. Ranallo listed accomplishments of the TSGA since its founding in 2014. TSGA formed a pediatric clinic network in 2015, supported the development of international clinical guidelines in 2016, sponsored an international research meeting in 2018, and formed an adult clinical network in 2020. In addition, TSGA championed the development of the InsighTS (Inspiring New Science in Guiding Healthcare for Turner Syndrome) Registry for research in 2020, and it plans to sponsor a meeting to update the international guidelines in 2022.

Ms. Ranallo closed her presentation with a video featuring comments about infertility from young women with Turner syndrome.

VI. RADx-UNDERSERVED POPULATIONS RETURN-TO-SCHOOL INITIATIVE

Sonia Lee, Ph.D., Acting Branch Chief, Maternal and Pediatric Infectious Disease Branch, NICHD, recalled that on March 13, 2020, NICHD asked all of its staff to work at home as COVID-19 began rapidly spreading throughout the United States. Many school systems sent their students home around that time. In September 2021, efforts are underway to return all children to in-person schooling safely.

According to the Centers for Disease Control and Prevention (CDC), the number of COVID-19 cases in children increased steadily from the spring of 2020 until early 2021. Rates then dropped before rising again in the summer of 2021.

Children need to be in schools and childcare settings in person, because these institutions provide services that are fundamental to child and adolescent development and well-being. In addition to providing academic instruction, schools help students develop social and emotional skills and provide reliable nutrition, mental and physical health services, and physical activity opportunities.

NIH launched RADx-Underserved Populations (RADx-UP) to enhance COVID-19 testing among underserved and vulnerable populations across the United States. The RADx-UP Return-to-School program is developing and testing COVID-19 diagnostic testing approaches to safely return children and staff to in-person school settings in underserved and vulnerable communities. In April 2021, RADx-UP awarded $33 million to eight sites for 2-year projects. In June and July 2021, the program awarded another $23 million to eight additional sites. All sites are testing

strategies for schools to combine frequent COVID-19 testing with proven safety measures to reduce the spread of COVID-19.

The health disparity and vulnerable populations in these projects include groups with low socioeconomic status, as well as Hispanic, Asian American, African American, rural, and American Indian and Alaska Native populations. The projects are evenly spread among elementary, middle, and high schools, with most projects taking place in public schools. However, a few projects are occurring in early childhood education sites, tribal schools, special education programs, and charter schools.

Dr. Lee described several of these projects. For example, one project focuses on children with complex health needs that make masking and physical distancing challenging. Another project is working with African American communities to keep children safely in school with masking and to shorten quarantine times when students are exposed to COVID-19. Two projects are addressing health disparities in children with intellectual and developmental disabilities who have difficulty wearing masks and staying distant consistently.

A workshop on August 9, 2021, gathered awardees and others conducting school-based research on COVID-19 diagnostic testing to learn from each other and discuss the state of their research projects. The videocast of this workshop will be posted to the NIH website soon. Some of the lessons learned to date include that testing in schools is feasible and can be implemented with strong support from communities and schools and with continual engagement and outreach. In addition, mitigation strategies allow schools to keep numbers of positive test results and levels of secondary transmission low. Some research gaps that Dr. Lee hoped the program would address include the impact of the delta variant and vaccine hesitancy, as well as optimal strategies for COVID-19 testing in school children with IDDs.

Remote learning has highlighted inequities in education that have had a detrimental impact on many students from underserved and vulnerable communities and exacerbated the mental health crisis among children and adolescents. A multipronged layered approach to keep children safely in school includes universal masking, vaccination for those who are eligible, appropriate ventilation, COVID-19 testing, contact tracing, quarantining, physical distancing, and routine cleaning and disinfection. Communication and coordination with health authorities is necessary to monitor community transmission, vaccination coverage, screening, testing, and outbreaks and to update the guidance for schools and families accordingly.

Discussion

Dr. Barkin applauded Dr. Lee and NICHD for creating this rapid but thoughtful research program that allows agile responsiveness to conditions affecting children now. She asked whether the Return-to-School initiative will address the strategies, in addition to testing, needed to return children safely to school, such as vaccination, masking, and ventilation. Dr. Lee said that schools are using different testing strategies. Projects are determining, for example, whether to screen asymptomatic students or to test only students with symptoms. Data from the projects are reviewed every month to try to provide rapid answers to questions about safe in-person schooling. The studies are using testing with other strategies to return children to in-person

learning and foster trust in parents and communities that children are in the best place for their education.

Dr. Wong noted that, according to anecdotal reports, families in states with low vaccination rates and no mask mandates are transferring their children to private schools that can implement these protocols. Dr. Lee explained that all RADx-UP projects are in underserved and vulnerable communities, and some charter schools and private schools serve these communities.

Alison Cernich, Ph.D., deputy director of NICHD, explained that the RADx-UP Return-to-School program focuses on testing. In addition, other activities led by CDC and other components of the Department of Health and Human Services are collecting data from private schools, and RADx-UP investigators can use those data for comparisons.

Dr. Wynshaw-Boris commented that if NICHD collects data on private schools that are following CDC guidelines, it needs to show the impact in the same community of following or not following these guidelines. Dr. Lee said that safe return to school is not an appropriate subject of a clinical trial, because schools are constantly changing their approaches and different children are spending time at home and then returning to school. This research needs to be conducted in real-world settings, and mitigation strategies in private schools and other settings need to be compared in underserved and vulnerable populations.

Dr. Rowitch noted the need to eventually assess the long-term effects of the COVID-19 pandemic. In addition, many countries are approaching in-person schooling in different ways, and Dr. Rowitch wondered whether NICHD plans to compare the effects of these approaches. Dr. Lee agreed that comparing the effects of the approaches used in different countries would be valuable. Some RADx-UP projects are collecting data on the effects of the pandemic on social, behavioral, and mental health, but answering questions about the long-term effects of the pandemic will take time.

Dr. Lang asked whether the Return-to-School program will study ways to combat disinformation campaigns, which appear to affect individual decisions. Dr. Lee replied that engaging community members in research requires combating disinformation. Some of the Return-to-School projects are doing this, and other RADx-UP studies are addressing vaccine hesitancy. Dr. Lang noted that disinformation will always exist and recommended that NICHD try to learn how to combat disinformation as it arises during the pandemic.

VII. COMMENTS FROM RETIRING MEMBERS

Dr. Bianchi asked two retiring NACHHD Council members to reflect on their service to the Council.

Dr. Sohn thanked NICHD leaders for the opportunity to serve on this Council and said that working with staff and other Council members had been a privilege. She was pleased with the changes in the DIR within her 3-year term. However, as COVID-19 has reminded everyone, infectious diseases respect no borders, and NIH needs to fund and share scientific advances to combat these diseases. Dr. Sohn was grateful that her final Council meeting would include a

review of three concepts that reflect NICHD's commitment to advancing global health and science. She was confident that NICHD will continue to extend the reach of its intramural and extramural research to benefit pregnant women, children, and adolescents around the world. Dr. Bianchi thanked Dr. Sohn for her dedication, engagement, and wisdom.

Dr. Bookheimer thanked NICHD for the opportunity to serve on the NACHHD Council, which has been a great honor. She appreciated the opportunity to contribute to NICHD's strategic plan by emphasizing the importance of research on children with IDD. She hoped that NICHD would maintain a focus on IDD throughout the lifespan in its intramural and extramural research. Although other ICs fund this type of research, none is dedicated to this cause. Dr. Bookheimer also hoped that new Council members will also represent the IDD community to ensure that this aspect of NICHD's mission is not forgotten. She thanked Dr. Bianchi and Dr. McBain for the transformative changes at NICHD, especially in the DIR. Overcoming equity and diversity challenges is difficult, but Dr. Bianchi and Dr. McBain showed that new leadership and dedication can change experiences for women and people of color, and Dr. Bookheimer sensed a new optimism and enthusiasm at the institute. Dr. Bianchi thanked Dr. Bookheimer for her contributions to the NICHD strategic plan and emphasized the importance for the institute of hearing from the experts on the NACHHD Council.

VIII. CONCEPT CLEARANCE

The NACHHD Council reviewed the following four concepts and voted to approve each one:

- **Prevention Research from Human Milk to the Origins of Disease and Development in the Life Course (The Primordial Project)** (Ashley Vargas, Ph.D., M.P.H., RDN, Pediatric Growth and Nutrition Branch)
- **Global Network for Women's and Children's Health Research** (Andrew Bremer, M.D., Ph.D., Pediatric Growth and Nutrition Branch)
- **Prevention and Treatment through a Comprehensive Care Continuum for HIV-affected Adolescents in Resource Constrained Settings (PATC3H)** (Bill G. Kapogiannis, M.D., Maternal and Pediatric Infectious Disease Branch)
- **NICHD Domestic & International Pediatric & Maternal HIV & Other High-Priority Infectious Diseases Clinical Studies Network** (Jack Moye, M.D., Maternal and Pediatric Infectious Disease Branch)

Global Network for Women's and Children's Health Research

Dr. Tita said that this network has done a wonderful job in a cost-effective way and has led to training and capacity building, including for some individuals who have become public health leaders. He asked about planned changes to the program to optimize its work. Dr. Bremer reported that network investigators responded to the COVID-19 pandemic in extraordinary ways and will continue to work with partners to respond to emerging needs.

Dr. Resnick pointed out that networks that have been in place for a long time need additional infrastructure to support the use of different types of data collection processes and data. Dr. Bremer replied that NICHD is working to make network data accessible to other researchers by, for example, using common data elements and leveraging data from other studies not only by NICHD networks but also by NIH and other federal partners.

PATC3H

Dr. Sohn commented that when PATC3H was initially established, investigators from eight groups quickly started working together, and she hoped that this collaboration would continue. Many NICHD priority populations, including adolescents and young women in sub-Saharan Africa, young men who have sex with men, and transgender people, lack access to HIV testing and HIV/AIDS care services. Dr. Sohn suggested that NICHD acknowledge the setback to HIV progress that resulted from the COVID-19 pandemic and the need to close this gap again. Dr. Kapogiannis said that the needs of vulnerable populations are in the scope of PATC3H.

NICHD Domestic & International Pediatric & Maternal HIV & Other High-Priority Infectious Diseases Clinical Studies Network

Dr. Sohn asked about planned changes to ensure that this network, which has been in existence for some time, remains responsive to the changes that have resulted from the COVID-19 pandemic. Dr. Moye replied that the network sites are continuously evaluated, and the program adds and removes sites based on NICHD's needs and their performance. NICHD is increasingly contending with requirements for monitoring and regulatory submission activity that support new drug approvals for anti-HIV agents in this population.

IX. ADJOURNMENT

Dr. Bianchi adjourned the closed session on Day 1 at 4:20 p.m.

X. CLOSED SESSION:

This portion of the meeting is closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

XI. REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and approved 522 HD-primary applications requesting *$179,353,361* in direct costs and $*253,296,981* in total costs.

XII. ADJOURNMENT

There being no further business, the meeting adjourned at 5:00 p.m. on Friday, September 10, 2021. The next meeting, which will also be virtual, is scheduled for January 11–12, 2022.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[2]

Diana W. Bianchi, M.D. Chair, National Advisory Child Health and Human Development Council Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development	Date

Dennis Twombly, Ph.D. Acting Associate Director, Division of Extramural Activities, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development	Date

Attachment: Council Roster

[2] These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.