NICHD-supported training and science: The role of simulation models to improve care for adolescents and young adults affected by HIV

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Harvard University Center for AIDS Research,
International Maternal Pediatric AIDS Clinical Trials Network,
International Epidemiology Databases to Evaluate AIDS,
Elizabeth Glaser Pediatric AIDS Foundation

Disclosures

- None

Roadmap

- Snapshot of HIV science
- NICHD-supported training and science
- Projecting clinical and economic impact of policies to improve care for adolescents affected by HIV
- Voice of the participant

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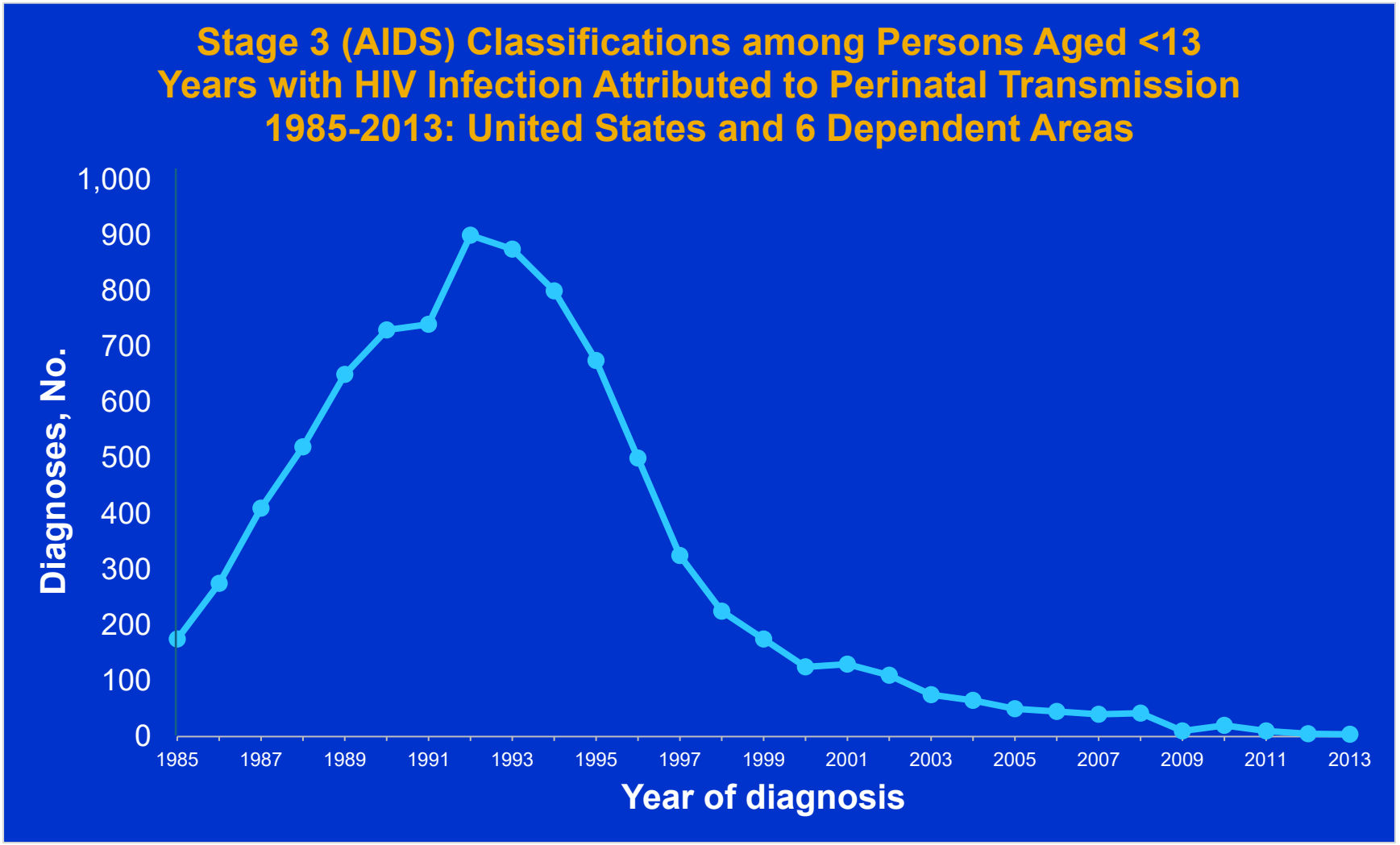
United States: “Virtual Elimination” of pediatric HIV since 1994



http://www.cdc.gov/hiv/library/slideSets/index.html

Antiretroviral therapy (ART) is well tolerated and effective

- Life expectancy is virtually the same as without HIV

Treating HIV prevents HIV

- Those who are virologically suppressed cannot transmit HIV sexually to others

CDC 2016

Antiretroviral medications can prevent HIV infection

- New recommendation to inform all sexually active adults and adolescents about HIV pre-exposure prophylaxis (PrEP)

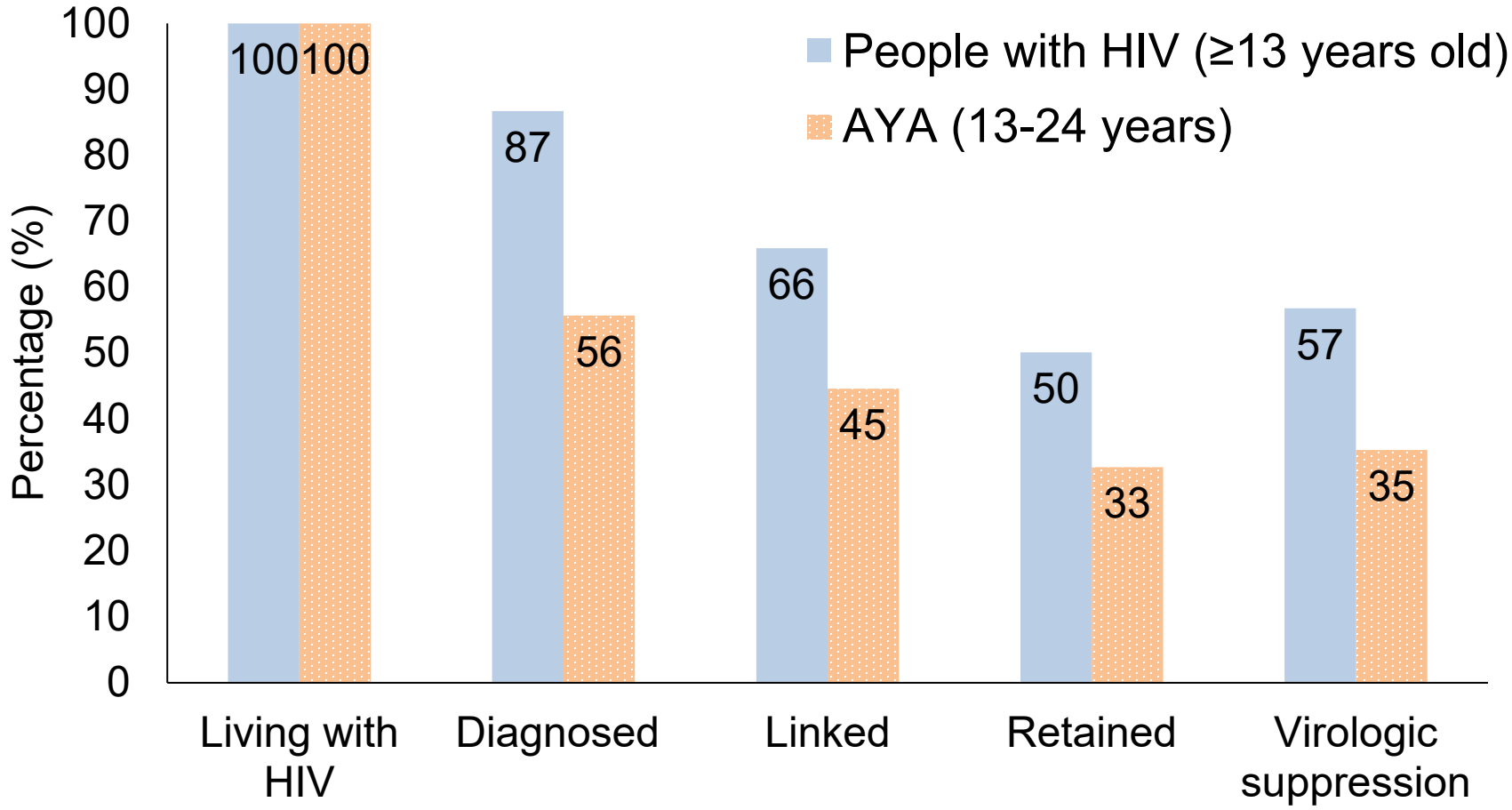
What about a vaccine or a cure?

- All HIV vaccines in development are in early-stage trials
- Exciting research advancing towards a functional cure
  - Broadly neutralizing antibodies among adults newly diagnosed
  - Very early antiretroviral therapy in infants may limit the size of the HIV reservoir, leading to the potential for ART-free remission, where the virus doesn't come back quickly if ART is stopped

  (IMPAACT P1115)

Gunst *Nature Medicine* 2023; Persaud *Lancet HIV* 2023

AYA with HIV have poorer HIV care continuum outcomes compared to adults



CDC 2019 data (reported in 2021)

The highest rate of onward HIV transmissions by age arises from AYA

Age group (years)	Transmissions generated, annual no. (%)	Transmission rate per 100 PYs
13-24	3,300 (8.5)	5.1
25-34	7,300 (19.0)	4.6
35-44	8,400 (21.8)	3.9
45-54	8,200 (21.3)	3.2
≥ 55	11,400 (29.4)	2.8
Total	38,700 (100)	3.5

Li *et al., Morb Mortal Wkly Rep* 2019 (2016 data)

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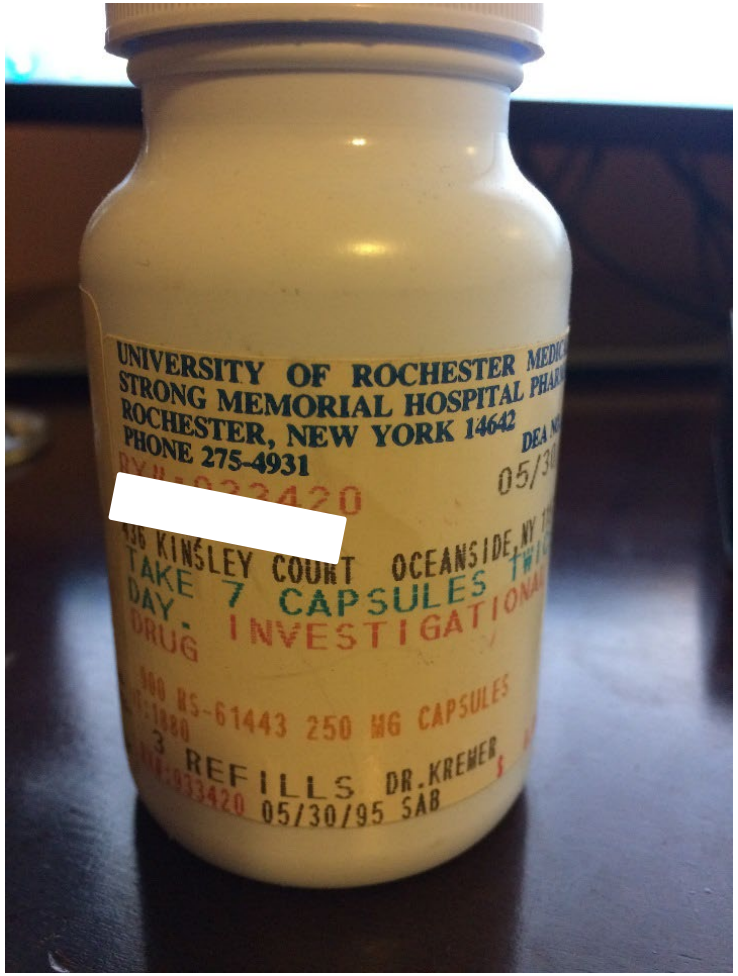
Early experience with how health policies impact individual people

The transformative power of medical research



NICHD-supported training

- NIAID T32 — HIV testing among US youth — **2014**
  - NIH Loan Repayment Program (LRP)
- Early career investigator support — ATN, IMPAACT, IeDEA, PHACS, HIVRN, CFAR — **2015-2017**
  - NIH Loan Repayment Program (LRP)
- NICHD K08 — HIV testing and PrEP US young MSM — **2018**
  - NIH Loan Repayment Program (LRP)
- NICHD R01 — Novel medications for youth in South Africa — **2022**
  - NIH Early Career Reviewer (ECR) Program
- ATN Modeling Core renewed — **2023**
  - NICHD Critical Life Event Supplement

Gifted mentors




ATN: Adolescent Medicine Trials Network for HIV/AIDS Interventions
IMPAACT: International Maternal, Pediatric, Adolescent AIDS Clinical Trials Network
IeDEA: International Epidemiology Databases to Evaluate AIDS
PHACS: Pediatric HIV/AIDS Cohort Study
HIVRN: HIV Research Network
CFAR: Centers for AIDS Research

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Simulation model-based analyses

- Balance of health benefits, risks, and costs
- Decisions must be made in the absence of ‘perfect’ data
  - Long follow-up or large sample sizes needed
  - Ethical and feasibility concerns
  - Difficulty ascertaining key outcomes (e.g., for those not in care)
  - Resources everywhere are constrained; costs are critical for implementation

Cost-effectiveness analysis

- Cost-effective ≠ saves money
- Cost-effective ≠ cheap

- More effective interventions are usually more costly
  - Is the additional benefit worth the additional cost?

Cost-effectiveness of Preventing AIDS Complications (CEPAC) group

- Monte Carlo simulation models (individual people)
  - Diagnosis, linkage, retention, re-engagement, ART use, opportunistic infections, mortality
  - Healthcare costs: medications, lab testing, clinical care
  - Data from trials, cohorts, and programs
- Adults, pregnant people and children, adolescents, comorbidities, aging



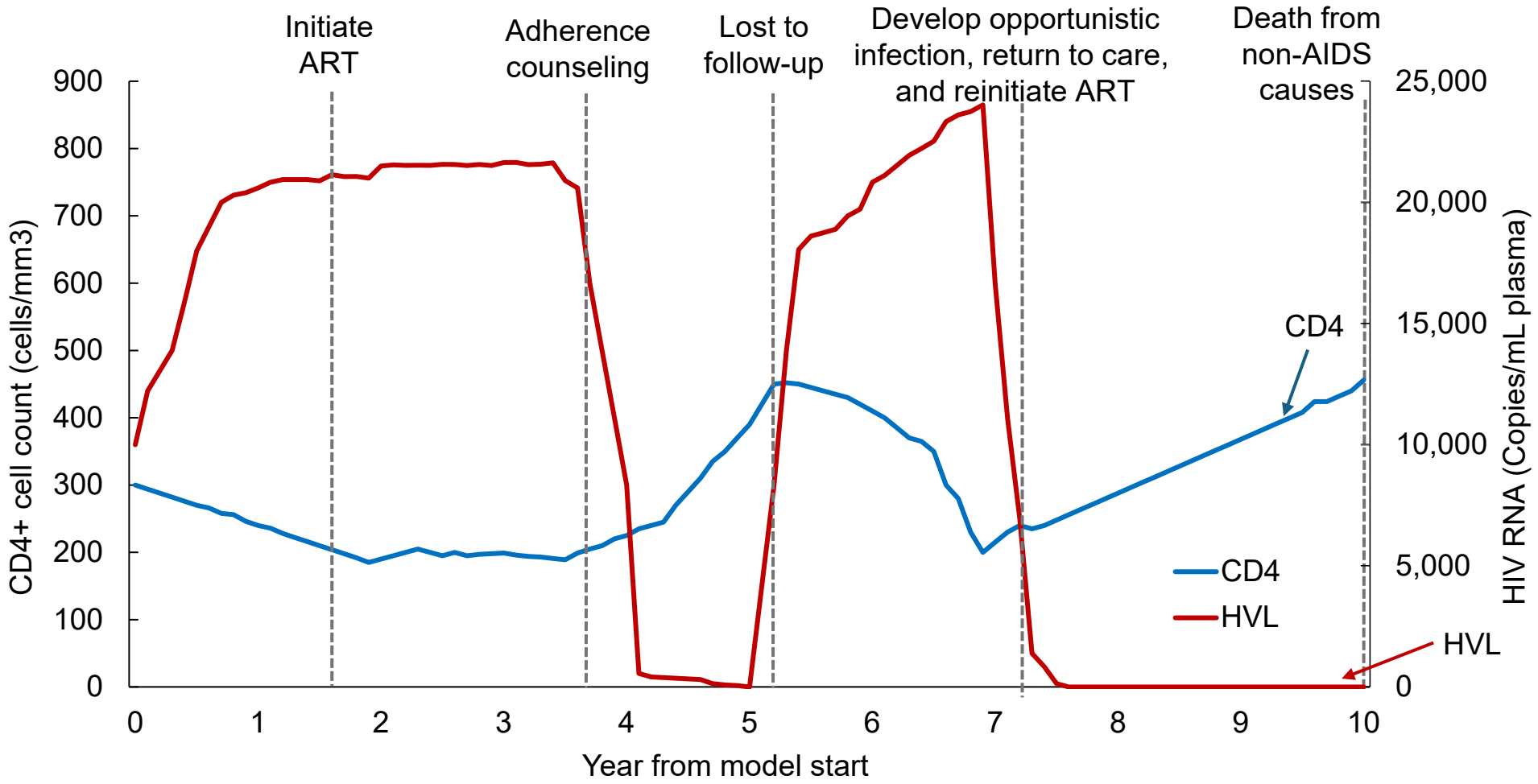




Freedberg *JAMA* 1998, Walensky *NEJM* 2005, Ciaranello *AIDS* 2008, Hyle *PLoS Med* 2014, Reddy *J Inf Dis* 2016, Neilan *JAMA Pediatrics* 2017; Dugdale *Ann Int Med* 2019

NIAID T32: Developing an adolescent-focused simulation model

- Structure allowing ART adherence and engagement in care to vary by age and over time



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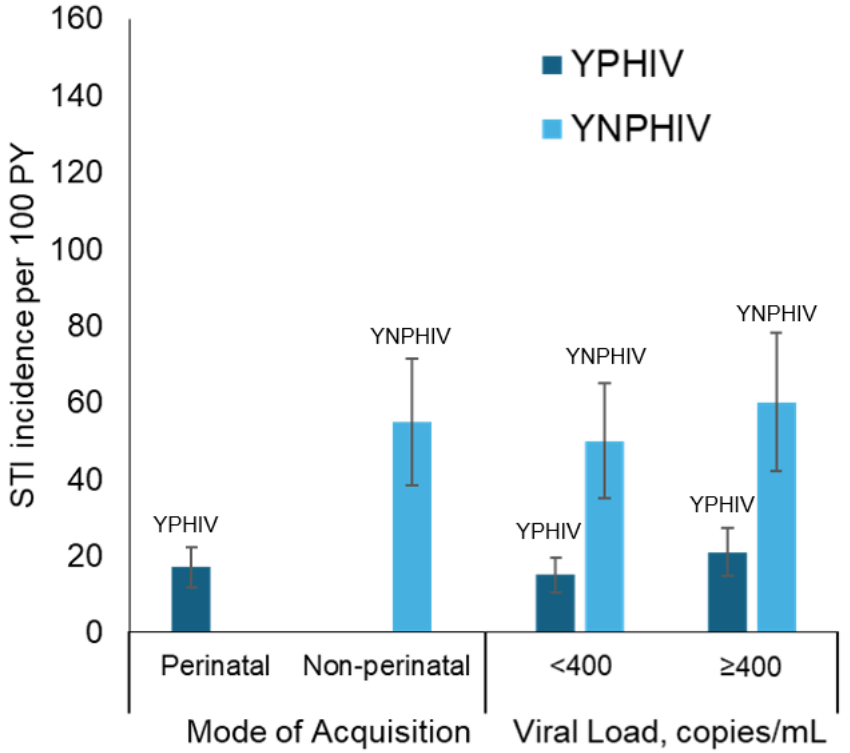
Data for model inputs
NICHD Data and Specimen Hub (DASH)

- Sexually transmitted infections in YHIV in three completed ATN studies
  - YNPHIV had higher rates of STIs than YHIV
  - Both groups had higher rates of STIs when at higher viral loads

- New method to address missing dates of STI diagnoses
  - Maximum likelihood estimator, when exact event times are unknown, may be more accurate than the crude incidence rate estimator



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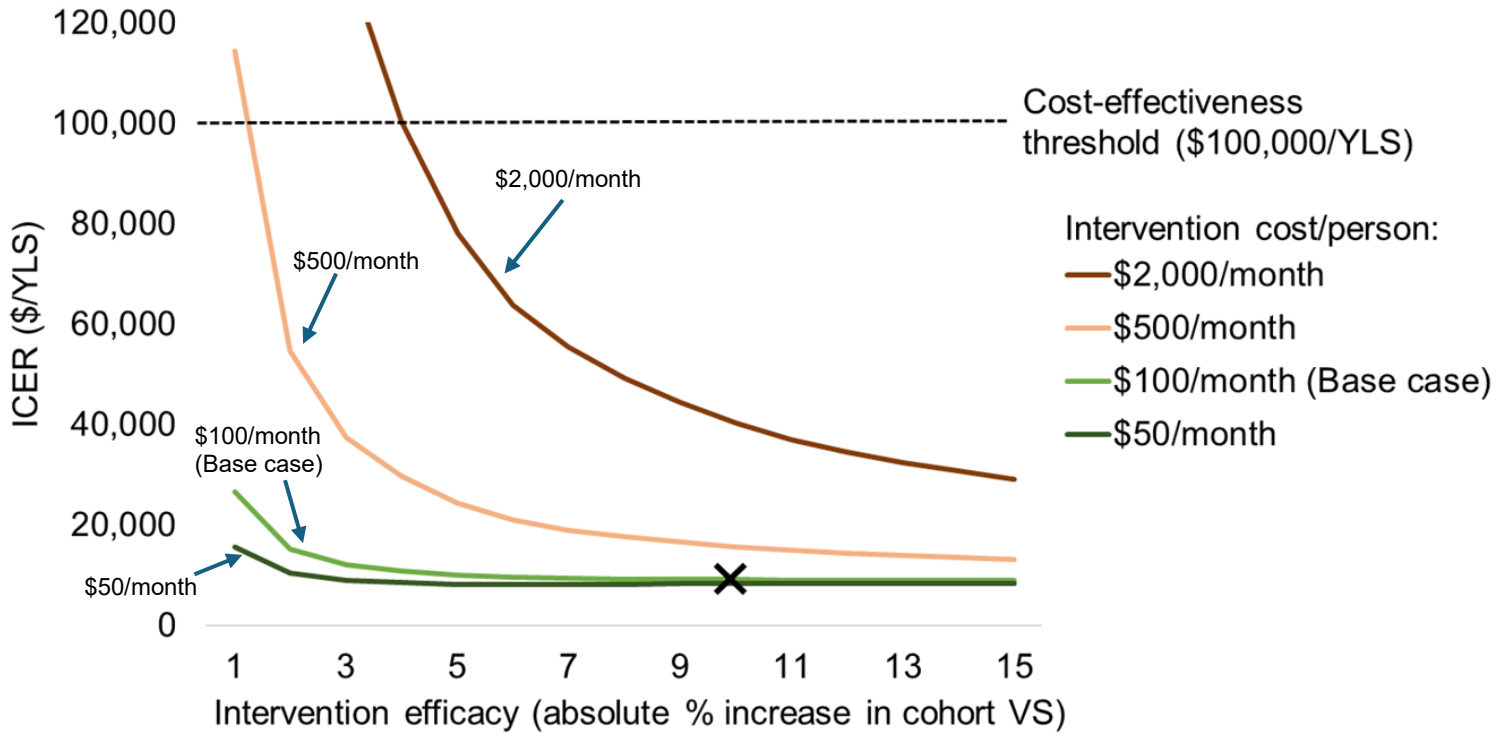
DeMonte JB, Neilan AM, Loop MS, Ciaranello AL, Hudgens MG. *Annals of Epidemiology*, 2021

ATN Modeling Core: Modeling cost-effectiveness of adherence interventions

- Even adherence interventions generating small improvements in virologic suppression would improve clinical outcomes and may be cost-effective



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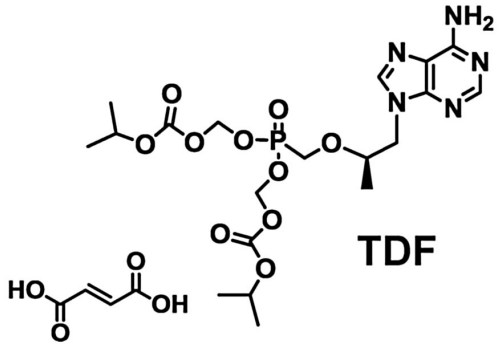
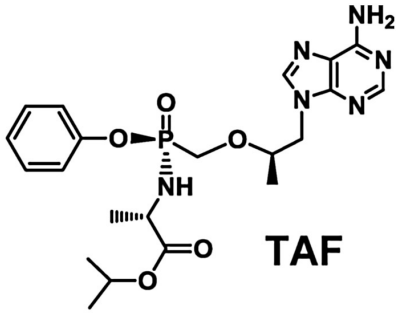
Currently three FDA approved options Pre-exposure Prophylaxis (PrEP)

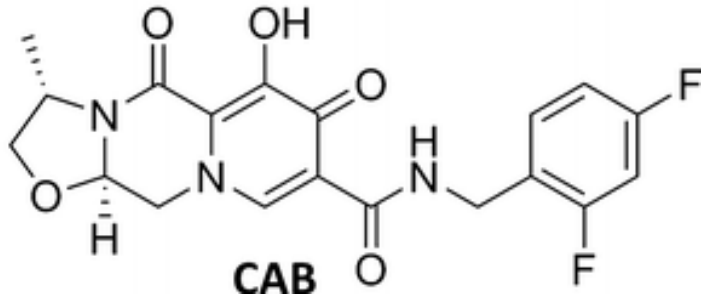
- Fixed-dose combination pills approved for daily oral PrEP in the US
  - Tenofovir disoproxil fumarate + emtricitabine (TDF-FTC)
  - Tenofovir alafenamide + emtricitabine (TAF-FTC)
- Long-acting injectable cabotegravir (CAB-LA)
- Drug prices vary widely:
  - ≤$160 annually for generic oral PrEP
  - ≥$18,000 annually for branded oral or injectable PrEP



TDF



TAF



CAB

National Acquisition Center Federal Supply Schedule U.S. Department of Veterans Affairs 2023
Mark Cuban CostPlus Drug Company 2023

NICHD K08: Generic oral PrEP would save both lives and money among YMSM

- Post-study analysis of ATN 110/113: Daily oral tenofovir-based PrEP among young men who have sex with men (YMSM) in the US
- Question: How would oral tenofovir-based PrEP compare to annual HIV screening alone among YMSM given high discontinuation and low adherence to PrEP among YMSM?
- Conclusion: At generic drug price, oral PrEP would be cost-saving among YMSM over a range of HIV incidences

Amick AM*, Eskibozkurt E*, Hosek S, Flanagan C, Landovitz RJ, Freedberg KA, Wilson CM, Weinstein MC, Paltiel AD, Ciaranello AL, Neilan AM. *Clin Infect Dis*. 2023.

NICHD K08: Long-acting injectable PrEP

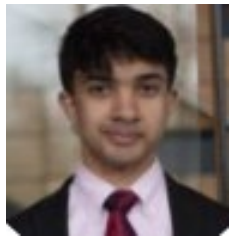
- HIV Prevention Trials Network (HPTN) 083
  - Long-acting injectable cabotegravir PrEP (CAB-LA)
  - Administered every 2 months
  - CAB-LA vs. daily oral PrEP: 69% risk reduction
- Question: How much should we be willing to pay for the improved efficacy of CAB-LA over daily oral PrEP?
  - Price not yet announced at the time
- Conclusion: <$7,000 annually given the availability of a highly effective oral generic alternative in the US

Neilan AM, Landovitz RJ, Le MH, Grinsztejn B, Freedberg KA McCauley M, Wattananimitgul N, Cohen MS, Ciaranello AL, Clement ME, Reddy KP, Hyle EP, Paltiel AD, Walensky RP. *Ann Int Med* 2022

NICHD R01: Injectable cabotegravir for adolescent girls and young women

- Collaboration Desmonde Tutu Health Foundation
  - CAB-LA not yet available, price unknown
  - Published data: CAB-LA vs. daily oral PrEP: 92% risk reduction in women in sub-Saharan Africa
- Question: How much should we be willing to pay for the improved efficacy of CAB-LA over daily oral PrEP in adolescent girls and young women?
- Preliminary conclusions: CAB-LA should be priced <2x oral PrEP to be cost-effective

DESMOND TUTU HEALTH FOUNDATION



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Projecting the potential increase in HIV transmissions due to "*Braidwood*"

- In 2022, a US federal court ruled against requiring health insurers to cover HIV PrEP under the Affordable Care Act
- We estimated that for every 10% decrease in PrEP coverage resulting from this ruling among US men who have sex with men, an additional 1,140 HIV infections in MSM would result in the following year
- Cited in
  - NYTimes within 24 hours
  - 2 amicus briefs
  - Top 15 papers in IDSA journals in 2023

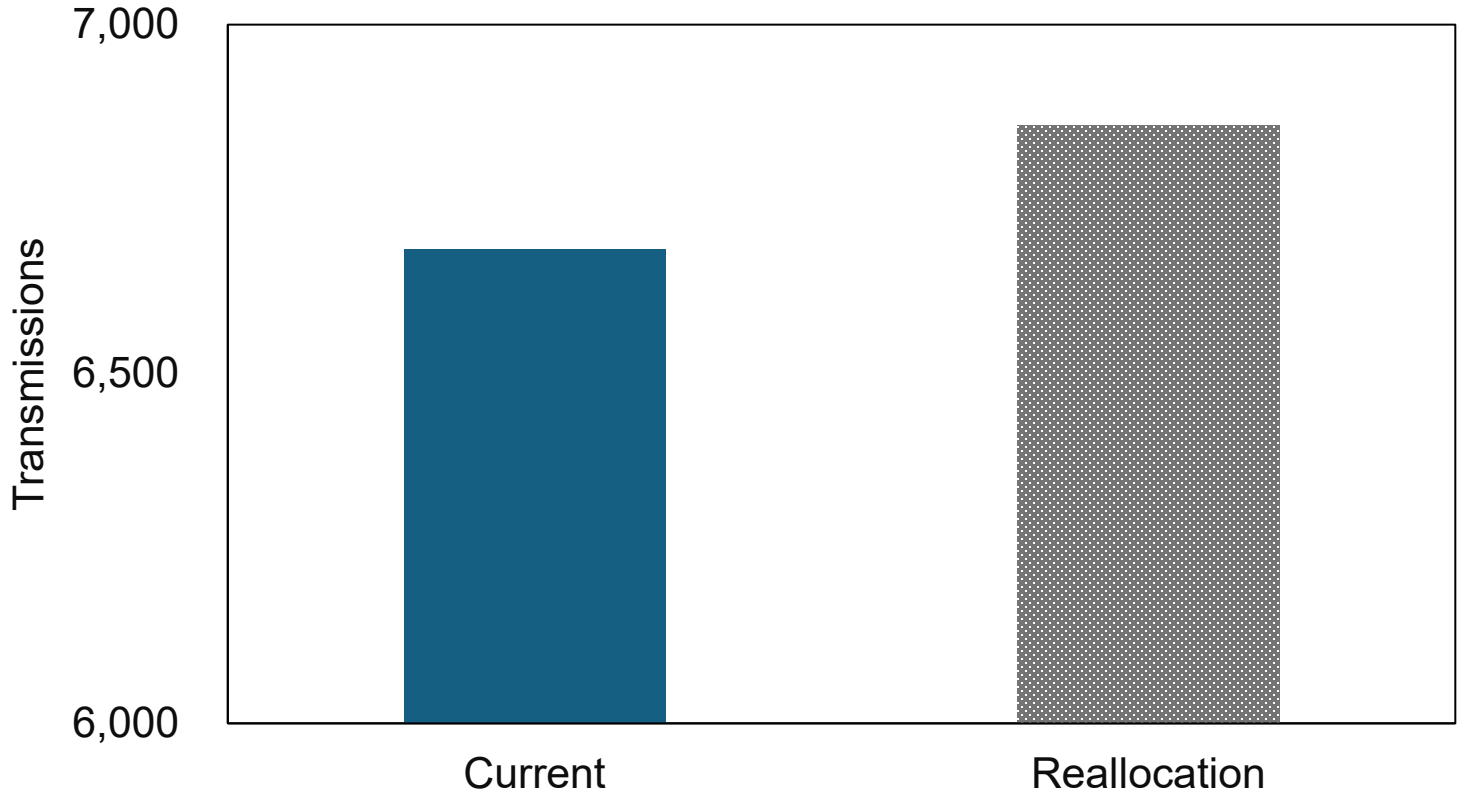

The New York Times

Federal Judge Strikes Down Obamacare Requirement for Free Preventive Care

Paltiel AD, Ahmed AR, Jin EY, McNamara M, Freedberg KA, Neilan AM, Gonsalves GS. *Open Forum Infect Dis,* 2023

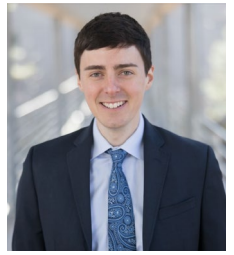

Tennessee Blocks Millions of Dollars in HIV Funding for Marginalized Groups
THE TENNESSEAN
Here's how Tennessee's health commissioner addressed shunned CDC grants for HIV prevention
Local HIV Prevention Orgs Adapt in the Wake of State Funding Cuts
NASHVILLE
FRIENDS FOR ALL

Funding reallocation would lead to **180 additional HIV infections in Tennessee** over 10 years



FRIENDS FOR ALL

NASHVILLE CARES



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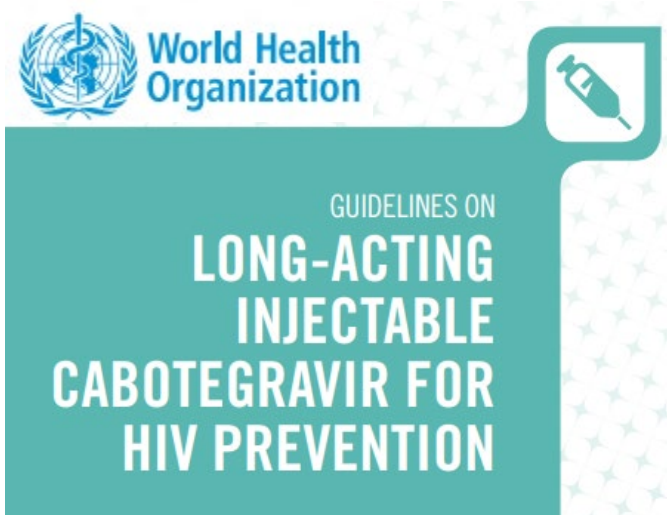
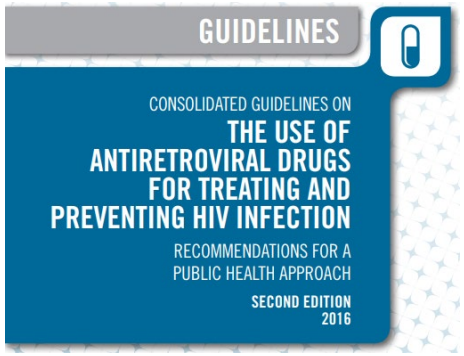
Informing Guidelines

2020 CDC	Modeling adherence interventions	*AIDS Behavior* 2021
2022 HHS	STI rates in US youth with HIV	*STDs* 2022
	Modeling adherence interventions	*AIDS Behavior* 2021
2022 WHO	Cabotegravir PrEP	*Annals Int Med* 2022





Special Considerations for Antiretroviral Therapy Use in Adolescents With HIV

Important next steps

- NICHD R01: Clinical and economic value of long-acting injectable antiretrovirals among adolescents with and without HIV in South Africa
- ATN Modeling Core: Lifetime costs of HIV infection among youth with HIV, value of information, trial-based analyses
- Trainee opportunities and current policy issues
  - Examples: Implications of cuts to PEPFAR funding

Conclusions

- Simulation modeling and cost-effectiveness provide uniquely valuable evidence to inform health policy
- The breadth and depth of NIH and NICHD support for early-stage investigators is vital to maintain a strong pipeline of clinician investigators
- NICHD-supported research in HIV has dramatically improved lives and informed health policy worldwide

Growing Adolescent Team

- CEPAC Research Group – Adolescent Collaborators
  - Ali Ahmed, Allison Agwu, Alyssa Amick, Ingrid Bassett, Audrey Bangs, Sayali Bhalerao, Ethan Borre, Alex Bulteel, Ravi Brenner, Andrea Ciaranello, Wanyi Chen, Kevin Chi, Caitlin Dugdale, Ege Eskibozkurt, Clare Flanagan, Julia Foote, Kenneth Freedberg, John Giardina, Elena Jin, Michelle Jones, Emily Hyle, Simeng Li, Kunjal Patel, David Paltiel, Krishna Reddy, Fatma Shebl, Virginia Talbot, Sujata Tewari, Ogochukwu Ufio, Rochelle Walensky, Milton Weinstein
- Desmond Tutu Health Foundation
  - Linda Gail Bekker, Catherine Orrell, Melissa Walker
- Adolescent Medicine Trials Network for HIV/AIDS Interventions Modeling Core

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  - NICHD R01 HD111355, K08 HD094638
  - Adolescent Medicine Trials Network for HIV/AIDS Interventions (UM2 HD111102)
  - NICHD CEPAC Pediatrics R01HD079214 (PI Ciaranello)
  - NIAID CEPAC US R01 AI042006 (PI Freedberg)
  - International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT)
  - International Epidemiology Databases to Evaluate AIDS (IeDEA)
  - Elizabeth Glaser Pediatric AIDS Foundation
  - MGH Claflin Distinguished Scholars Award
  - MGH Department of Medicine Transformative Scholars Award
  - Morton N. Swartz Transformative Scholar Award in Infectious Diseases
  - Harvard University Center for AIDS Research
  - Harvard Medical School Eleanor and Miles Shore Scholars in Medicine

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