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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Current and past support for Dr. Neilan from:
NICHD (K08 HD094638, R01 HD111355)
Adolescent Medicine Trials Network for HIV/AIDS Interventions (UM2HD111102)
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
Roadmap

• **Snapshot of HIV science**
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United States: “Virtual Elimination” of pediatric HIV since 1994

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

![Graph showing percentages of HIV care continuum outcomes for People with HIV (≥13 years old) and AYA (13-24 years)]

- Living with HIV: 100%
- Diagnosed: 87%
- Linked: 66%
- Retained: 50%
- Virologic suppression: 57%

CDC 2019 data (reported in 2021)
The highest rate of onward HIV transmissions by age arises from AYA

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

Li et al., *Morb Mortal Wkly Rep* 2019 (2016 data)
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Early experience with how health policies impact individual people

Give thanks. Give life.
The transformative power of medical research
NICHD-supported training

NIAID T32
HIV testing among US youth
2014

Early career investigator support
ATN, IMPAACT, IeDEA, PHACS, HIVRN, CFAR
2015-2017

NICHD K08
HIV testing and PrEP
US young MSM
2018

NICHD R01
Novel medications for youth in South Africa
2022

ATN Modeling Core renewed
2023

NIH Loan Repayment Program (LRP)

NIH Loan Repayment Program (LRP)

NIH Loan Repayment Program (LRP)

NIH Early Career Reviewer (ECR) Program

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

NIAID T32: Developing an adolescent-focused simulation model

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

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


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.

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
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
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

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
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

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

<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Topic Description</th>
<th>Journal/Year</th>
</tr>
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<tbody>
<tr>
<td>2020</td>
<td>CDC</td>
<td>Modeling adherence interventions</td>
<td>AIDS Behavior 2021</td>
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<tr>
<td>2022</td>
<td>HHS</td>
<td>STI rates in US youth with HIV</td>
<td>STDs 2022</td>
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<td></td>
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<td>Modeling adherence interventions</td>
<td>AIDS Behavior 2021</td>
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<tr>
<td>2022</td>
<td>WHO</td>
<td>Cabotegravir PrEP</td>
<td>Annals Int Med 2022</td>
</tr>
</tbody>
</table>
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
- Desmond Tutu Health Foundation
  - Linda Gail Bekker, Catherine Orrell, Melissa Walker
- Adolescent Medicine Trials Network for HIV/AIDS Interventions Modeling Core
Thank you

- CEPAC Adolescent Model past and current support:
  - 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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