HPTN 2023
State of the Network

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- Susan Eshleman
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78 Trials
ongoing or completed
172,000+
Study participants enrolled
800+ Publications
<table>
<thead>
<tr>
<th>Year</th>
<th>HPTN</th>
<th>Initiative</th>
<th>Details</th>
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</thead>
<tbody>
<tr>
<td>1993</td>
<td>IMC/HIVNET</td>
<td>Cates &amp; Self</td>
<td>Vaccines, Microbicides, MTCT, ART Prevention, STI Treatment, Substance Use, Behavioral Intervention</td>
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<td>1999</td>
<td>HPTN I</td>
<td>Cates &amp; Coates</td>
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<td>2006</td>
<td>HPTN II</td>
<td>Vermund &amp; Abdool-Karim</td>
<td>Vaccines, Microbicides, MTCT, TaSP (052), STI Treatment, Substance Use, Behavioral Structural Intervention</td>
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<td>2013</td>
<td>HPTN III</td>
<td>El-Sadr &amp; Cohen</td>
<td>Integrated Strategies: Biomedical, Behavioral, Structural, Oral PrEP, Alternate drugs, regimens, and formulations, Phase I to III</td>
</tr>
</tbody>
</table>
UNDETECTABLE  ≡  UNTRANSMITTABLE
The impact of Fast-Track

New HIV infections in low- and middle-income countries

AIDS-related deaths in low- and middle-income countries

- Red: Business as usual (no scale-up)
- Blue: Fast-Track results (rapid scale-up)
Two Points to Consider First

• HPTN/HVTN = The COVID Prevention Network (CovPN)
  - Moderna, Astra Zeneca, J&J, Novavax vaccines
  - mAbs from Lilly, Regeneron and Astra Zeneca

But.. Consider the HPTN/HVTN Opportunity Costs

Recent HVTN Vaccine Trials
- HIV vaccine development continues to prove VERY challenging
- Collaborative HVTN/HPTN bnAb research for next PrEP
- bnAb research informs vaccine development, long-term
Achieving Population Impact

Biomedical Interventions

Behavioral Interventions

Structural Interventions
Forward: 2023 Clinical Research Sites

- 68 HPTN Sites
- 13 Countries
- 22 African Sites
- 5 Asian Sites
- 30 North American Sites
- 11 South American Sites
NEXT in PrEP
CAB LA PrEP IS APPROVED in the U.S. – What’s Next?

• Open label extension (OLE) studies will estimate continued safety and protection, PK, resistance, and include pregnancy and adolescent substudies.

• ViiV is working to gain approval for PrEP in all HPTN 083 and HPTN 084 in participating countries; affordable access where it is awaiting approval BEYOND the U.S.

• New studies in development to examine effectiveness of CAB-LA among adolescents and PWID.

• New studies to explore different routes of administration (e.g., thigh). fewer injections/year and more.

• Combine cabotegravir-LA with contraceptives in future studies?
Pregnancy Sub-Study in HPTN 084 OLE

- Estimate the incidence of pregnancy among participants during the OLE period
- Evaluate safety and infant outcomes among pregnant participants
- Evaluate the PK of CAB LA among pregnant participants, combining blinded, unblinded and OLE periods
- Evaluate concentration in breastmilk and infants among women who receive CAB LA injections during pregnancy and/or the early post-partum period.
The HPTN/Gilead Collaboration: A New paradigm

- Lenacapavir, a first-in-class selective HIV capsid inhibitor, with subcutaneous injections every 6 months

- HPTN and Gilead will develop two companion studies in collaboration:
  - HPTN 102/Purpose 3: A lenacapavir Phase 2 PK, safety, acceptability in cis-gender women in the US
  - HPTN 103/Purpose 4: A phase 2 PK, safety, acceptability of lenacapavir in people who inject drugs (PWID) in the US
Phase 2 Open-label comparative randomized (1:1) crossover study of two 8-week on-demand open label product sequences comparing rectal and oral tenofovir-based PrEP

**Sample Size:** ~150 participants in the US assigned male at birth with a history of receptive anal intercourse and experience with douching, ≥18 years of age

**Study duration:** 19 weeks per participant; participant accrual approximately 9 months

**Regulatory Sponsor:** NIH

**Primary Objectives:**

- Safety and acceptability of the on-demand rectal TFV douche vs oral F/TDF tablet
- Study enrollment begins: Q4 2023,

**Challenges:** drug manufacturing expected to be complete summer 2023, concurrent forward movement related to data management, labs and site preparedness

**Speculation:** phase 2 complete (data analyzed) Q4 2025, so will there be a phase 3?
Broadly Neutralizing Antibodies for HIV Prevention
Broadly Neutralizing Antibodies

The transmitted-Founder virus

Escape virus

HIV-1

The initial neutralizing antibody response to HIV “autologous nAb”

Antibody

Continuum with 10~20% Broadly neutralizing antibodies
Antibody Mediated Prevention trials

VRC01 is a broadly neutralizing antibody (bNAb) which blocks the CD4 binding site on the HIV envelope.

- VRC01 was infused every 2 months x 10 to high-risk women (Africa) and MSM and transgender individuals (Americas) (n=4,600)
- Two doses of VRC01 were evaluated: 10 mg/kg and 30 mg/kg

VRC01 neutralized highly sensitive viruses, no effect on others
## bNAb PrEP Joint Studies

<table>
<thead>
<tr>
<th>Study (HVTN/HPTN)</th>
<th>Product(s)</th>
<th>Target</th>
<th>Route</th>
<th>Long-acting</th>
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</thead>
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<tr>
<td>703/081, 704/085</td>
<td>VRC01</td>
<td>CD4 binding site</td>
<td>IV</td>
<td></td>
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<tr>
<td>127/087</td>
<td>VRC07-523LS</td>
<td>CD4 binding site</td>
<td>IV, SC, IM</td>
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<tr>
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<td>PGT121, PGDM1400, 10-1074, VRC07-523LS</td>
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<td>CD4-bs + V3</td>
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<td>CD4-bs + V2+ V3</td>
<td>IV, SC</td>
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<tr>
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<td>VRC01.23LS, ePGDM1400v9LS, ePGT121v1LS</td>
<td>CD4-bs + V2+ V3</td>
<td>IV, SC</td>
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<tr>
<td>143/109</td>
<td>VRC01.23LS, PGDM1400LS, PGT121.414LS</td>
<td>CD4-bs + V2+ V3</td>
<td>IV</td>
<td>√</td>
</tr>
</tbody>
</table>
NIH Criteria for a bNab PreP Trial

• Pharmacology leads to a stable combination (i.e. no “tails”)
• A product manufacturer
• A commercial partner
• An ethical trial design
• Feasible implementation
Phase 2b, open label, randomized crossover study of DPP (co-formulated F/TDF+ ethynyl estradiol/levonorgestrel oral contraceptive pill (OCP), compared with the two tablets with daily oral F/TDF + OCP (2PR) for PrEP and pregnancy prevention in HIV-uninfected women

Sample Size: ~300 women 16-39 years (100 adolescents) for 48 weeks per participant

Regulatory Sponsor: Viatris

Primary Objective:

- Compare PrEP adherence to the DPP versus 2PR during a randomized crossover period

**Challenge: BE data is gatekeeper for availability of drug formulation**

Approval of DPP is through 503B pathway (bioequivalence data is sufficient)

BE 4 pilot starts late May. Results expected late Aug 2023

Pivotal BE: Results expected Q3 2024

Speculation: submissions (Q4 2024). Approval Q 4 2025?
Back to STIs and the HIV “Syndemic”

Primary & Secondary Syphilis: Reported Cases by Sex, Sex of Sex Partners, and HIV Status, 2021

Proportion of MSM with Primary and Secondary Syphilis, Urogenital GC, or Urogenital CT by HIV Status, STD Surveillance Network (SSuN), 2021

Among cases with reported HIV status, 44% among MSM were HIV+, compared with 38% among men with unknown sex of sex partners, 7.1% among men who have sex with women only, and 3.9% among women.

Percent with primary and secondary syphilis was higher for HIV+ compared with those not (12% vs 4.9%), similar to urogenital chlamydia (6.2% vs 5.4%) and gonorrhea (12% vs 7.8%)
A Phase II randomized, observer-blind, placebo-controlled study to assess efficacy of meningococcal Group B vaccine MenB+OMV NZ (Bexsero) in preventing gonococcal infection (DMID Protocol 19-0004/HPTN 108)


**Study design**
Phase II, randomised, observer-blind, placebo-controlled trial (USA and Thailand)

**Primary objective**
Bexsero efficacy in preventing urogenital and/or anorectal gonococcal infection

Subjects at risk of *N. gonorrhoeae* infection
N=~2200, aged 18–50 years

Recruiting estimated completion 2024
Target enrolment 2,200 to achieve 202 incident infections
Current enrolment 667 across 11 sites

3 HPTN Sites in the US and (soon) Malawi
Integrated Strategies
Integrating HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas: A Vanguard Study
HPTN 091: Study Status

• Enrollment was completed on 16 December 2022. 307 (99%) participants were enrolled in the study. Follow up is anticipated to end Q2 2024.

• An immediate vs deferred intervention study design.

• Sites have a process transitioning participants off the study and to local resources.

• The study has experience exceptional (>90%) retention.
INTEGRA: A Vanguard Study of Health Service Delivery in a Mobile Health Delivery Unit to Link Persons who Inject Drugs to Integrated Care and Prevention for Addiction, HIV, HCV and Primary Care
HPTN 094: Study Design

- A two-arm, individually randomized, controlled, open label study
- 450 participants (400 participants without HIV) allotted in 1:1 ratio to intervention and control arms, with a target of a minimum 25% women, a target of a minimum of 25% participants under 30 years of age and approximately 10% living with HIV

371 enrolled to date
Getting to Zero among Black MSM in the American South: Testing the Efficacy of an Integrated Strategy
HPTN 096: An Evolving Experimental Strategy

Integrated Strategy

Social Media

Health Equity

Peer Support

CRISP
Culturally Responsive Intersectional Stigma Prevention

CRISP Facility-Level Outcomes

Increased Number of Black MSM Clients/Patients at CRISP healthcare facilities

- Increased Viral Suppression in Black MSM
- Increased PrEP Prescriptions in Black MSM
Among young gay and bisexual males, HIV treatment and prevention are not reaching everyone equitably.

Declines in estimated new HIV infections among gay and bisexual males in the U.S., ages 13-24, by race/ethnicity, 2017-2021:

- **Black/African American**: 3,700 in 2017, 2,700 in 2021 (27% decrease)
- **Hispanic/Latino**: 2,200 in 2017, 1,400 in 2021 (36% decrease)
- **White**: 1,100 in 2017, 610 in 2021 (45% decrease)

*Data unavailable for other races/ethnicities in this age group.

Source: Centers for Disease Control and Prevention
New Approved Concepts

- **HPTN 111**: Uptake of HIV Self-testing and Linkage to Prevention and Care among Heterosexual Men Attending Barbershops in Uganda: A Cluster Randomized Trial

- **HPTN 112**: Improving HIV Prevention Among Heterosexual Men Seeking STI Services in Sub-Saharan Africa: Examining the Feasibility, Acceptability, and Associated Costs of a Systems-Navigator-Delivered Integrated Prevention Package

- **HPTN 113**: Double Prevention: A Vanguard Study of an Integrated Strategy of HIV PrEP and STI PEP for Young Latino Sexual Minority Men (SMM) in the Americas
Community Engagement is pivotal part of all HPTN studies.
A few examples:

• Advocacy for affordable post-trial access to CAB LA in countries where HPTN 083 and HPTN 084 are being conducted

• Participating in the development of all forthcoming HPTN research initiatives

• Authored “Including pregnant and breastfeeding people in trials of novel LAED PrEP agents – perspectives from sub-Saharan Africa community stakeholders” for JIAS Special Issue

• Community-led study branding HPTN 106 and the HPTN 096 “What I Want Most” campaign
Domestic Program established in 2010
  • 48 Scholars to date

International Program established in 2015
  • 15 Scholars to date

60+ Scholars since 2010 (some were in multiple cohorts)
  • 34% men; 66% women
  • 20 datasets: HPTN 037-HPTN 082
  • 50+ mentors

HPTN involvement
  • Protocol Team Members (HPTN 073, 078, 094, 096)
  • Protocol Team Leadership (HPTN 091, HPTN 096)
  • Memberships/Observerships: Black Caucus, Scientific Committees, and Working Groups
2022-2023 HPTN Scholars

Dr. Tina Herrera  
Dr. David Zelaya  
Dr. Donte Boyd  
Dr. Waru Gichane  
Dr. Sophia Zamudio-Haas  
Dr. Victoria Ndyanabangi  
Kudzai Hlahla
Acknowledgments

Thank you very much to all study participants, investigators and site staff, community groups, collaborators and funders

Overall support for the HIV Prevention Trials Network (HPTN) is provided by:

- National Institute of Allergy and Infectious Diseases (NIAID)
- Office of the Director (OD), National Institutes of Health (NIH)
- National Institute on Drug Abuse (NIDA)
- National Institute of Mental Health (NIMH)
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- ViiV Healthcare, Gilead Sciences, The Bill and Melinda Gates Foundation, and Viatris
- Collaborations with HVTN, ACTG, IAVI, AVAC and Rockefeller University

Award Numbers UM1AI068619 (HPTN Leadership and Operations Center), UM1AI068617 (HPTN Statistical and Data Management Center), and UM1AI068613 (HPTN Laboratory Center).