HPTN 2022
State of the Network

Myron S. Cohen, MD
Wafaa El-Sadr, MD, MPH
Principal Investigators, HPTN
Priority Areas as per RFA (2020-2027)

- Identify **novel ARV-based methods and delivery systems** for HIV prevention

- Develop **multi-purpose technologies (MPTs)** for HIV prevention as well as for contraception, prevention of other STIs

- Evaluate **broadly neutralizing antibodies (bnAbs)** alone or in combination that prevent HIV acquisition, in collaboration with the HVTN

- Design and conduct population-specific **integrated strategy studies** that combine biomedical, socio-behavioral and structural interventions for HIV prevention to maximize their effectiveness
Scientific Aims

• Develop new biomedical interventions:
  – Novel ARV methods & delivery systems
  – Multi-Purpose Technologies (MPTs)
  – Broadly neutralizing antibodies (bnAbs)

• Optimize integration of proven interventions to achieve high effectiveness and impact:
  – Biomedical
  – Socio-behavioral
  – Structural

Discovery

Impact
Clinical Research Sites

- 69 HPTN Sites
- 14 Countries
- 24 African Sites
- 4 Asian Sites
- 30 North American Sites
- 11 South American Sites
Network Structure – Leaders

Executive Committee (EC)
- Myron S. Cohen
- Wafaa El-Sadr
- Quarraisha Abdool Karim
- Chris Beyrer
- Sinead Delany-Moretlwe
- Deborah Donnell
- Susan Eshleman
- Sybil Hosek
- Raphael Landovitz
- Nyaradzo Mgodi
- David Serwadda
- Sten Vermund
- Nirupama Sista
- Melissa Turner
- Darrell Wheeler
- 2 NIH Representatives

Leadership and Operations Center (LOC) FHI 360
- Nirupama Sista

Statistical and Data Management Center (SDMC) SCHARP
- Deborah Donnell

Laboratory Center (LC) Johns Hopkins University
- Susan Eshleman
- Mark Marzinke
# Working Group Leadership

<table>
<thead>
<tr>
<th>Science Committees</th>
<th>Chair</th>
<th>Co-Chair</th>
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<tbody>
<tr>
<td>Adolescents at Risk</td>
<td>Audrey Pettifor</td>
<td>Linda-Gail Bekker</td>
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<tr>
<td>Sexual and Gender Minority</td>
<td>Kenneth Mayer</td>
<td>Nittaya Phanuphak</td>
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<tr>
<td>Substance Users</td>
<td>Steffanie Strathdee</td>
<td>Nabila El-Bassel</td>
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<td>Women at Risk</td>
<td>Ada Adimora</td>
<td>Philippa Musoke</td>
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<table>
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<tr>
<th>Working Groups</th>
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<tbody>
<tr>
<td>Biomedical Sciences</td>
<td>Jeanne Marrazzo</td>
<td>Joseph Eron</td>
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<tr>
<td>Community</td>
<td>Melissa Turner</td>
<td>Ntando Yola</td>
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<tr>
<td>Ethics</td>
<td>Jeremy Sugarman</td>
<td>Jerome Singh</td>
</tr>
<tr>
<td>Socio-Behavioral Sciences</td>
<td>Ariane van der Straten</td>
<td>Julie Pulerwitz</td>
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<th>Technical Liaisons</th>
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<tr>
<td>Susan Buchbinder, Connie Celum, Sharon Hillier</td>
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New ARVs for PrEP
**Research Summary**

**Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women**

**Clinical Problem:**

More than 5000 new HIV infections occur each day worldwide, despite the availability of effective preventive strategies. Daily oral tenofovir disoproxil fumarate/emtricitabine (TDF-FTC) is one option for pre-exposure prophylaxis, but long-acting regimens could help increase adherence and, therefore, efficacy.

**Clinical Trial:**

**Design:** An international phase 2b–3, randomized, double-blind, noninferiority trial was conducted to compare long-acting cabotegravir with daily TDF-FTC in adults at high risk for HIV infection.

**Intervention:** 4570 cisgender men and transgender women who have sex with men were assigned to receive long-acting intramuscular cabotegravir every 8 weeks plus oral placebo daily or placebo injection every 8 weeks plus oral TDF-FTC daily. The primary efficacy outcome was incident HIV infection.

**Results:**

- **Efficacy:** During a median follow-up of 1.4 years, long-acting cabotegravir was superior to daily TDF-FTC in preventing incident HIV infection.
- **Safety:** The occurrence of adverse events of grade 2 or higher — the primary safety outcome — did not differ substantially between the groups.

**Limitations and Remaining Questions:**

- Emergent strand-transfer inhibitor resistance was detected in 4 participants in the cabotegravir group, who acquired HIV infection; strategies are needed to prevent such resistance.
- The logistics of implementing cabotegravir-based prevention programs warrant further study.

**Conclusions:**

Injectable cabotegravir given every 8 weeks was superior to daily oral TDF-FTC for preventing HIV infection among high-risk cisgender men and transgender women who have sex with men.

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Cabotegravir for prevention of HIV-1 in women: results from HPTN 084, a phase III, randomised controlled trial


The Lancet, 2022-05-07, Volume 399, Issue 10337, Pages 1779-1789
• Open label extension (OLE) studies will estimate continued safety and protection, PK, resistance, etc., and include a 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 US
• 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.
HPTN-Gilead Collaboration

- Long-acting injectable drug developed by Gilead – lenacapavir, a first-in-class selective HIV capsid inhibitor, with sub-cutaneous injections every 6 months

- Gilead is pursuing simultaneous treatment and prevention studies, including two company sponsored efficacy studies for prevention

- 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
HPTN 102 & 103 - Gilead Purpose 3 & 4

Visit Schedule

Screen Day 1 W 4 W 8 W 13 W 26 W 39 W 52/ Day 1 W 13 W 26 W 39 W 52 W 65 W 78

Injection Schedule

ARM A
- Oral LEN on Days 1 and 2 + SC LEN every 26 weeks
- Daily oral F/TDF

ARM B
- Daily oral F/TDF
- Daily oral F/TDF

Approximately 1 year of randomized open-label study duration

Approximately 1.5 years of PK tail coverage for Arm A after completion of or early transition from 52 weeks of randomized open-label phase; continued access for Arm B
Broadly neutralizing antibodies for Prevention
Broadly Neutralizing Antibodies

The transmitted-Founder virus

Escape virus

HIV-1

Continuum with 10~20% Broadly neutralizing antibodies

Antibody

The initial neutralizing antibody response to HIV “autologous nAb”
Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition


**Prevention Efficacy Declines with Resistance**

<table>
<thead>
<tr>
<th>Resistance Level</th>
<th>Treatment arm</th>
<th>No. of HIV-1 Infections</th>
<th>No. of Person-Years</th>
<th>Rate per 100 Person-Years</th>
<th>PE (95% CI)</th>
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<tr>
<td>&lt;1 µg/ml</td>
<td>Control</td>
<td>19</td>
<td>2203</td>
<td>0.86</td>
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<td>VRC01 Pooled</td>
<td>9</td>
<td>4427</td>
<td>0.20</td>
<td>75.4 (45.5, 88.9)</td>
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<td></td>
<td>VRC01 10 mg/kg</td>
<td>4</td>
<td>2210</td>
<td>0.18</td>
<td>79.2 (39.1, 92.9)</td>
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<td></td>
<td>VRC01 30 mg/kg</td>
<td>5</td>
<td>2217</td>
<td>0.23</td>
<td>71.5 (23.3, 89.4)</td>
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<tr>
<td>1-3 µg/ml</td>
<td>Control</td>
<td>10</td>
<td>2203</td>
<td>0.45</td>
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<td></td>
<td>VRC01 Pooled</td>
<td>19</td>
<td>4427</td>
<td>0.43</td>
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<td>VRC01 10 mg/kg</td>
<td>13</td>
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<td>6</td>
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<td>0.27</td>
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<td>&gt;3 µg/ml</td>
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<td>2203</td>
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<td>2210</td>
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<td>VRC01 30 mg/kg</td>
<td>33</td>
<td>2217</td>
<td>1.49</td>
<td>5.8 (−55.1, 42.7)</td>
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Viruses are not getting significantly more resistant over time to most bnAbs

Differences of neutralization sensitivity between viruses over calendar time were evaluated using the Jonckheere-Terpstra test for trend.
Criteria for a bNab PrEP Product

- Breadth (90% coverage)?
- Potency (SubQ administration???)
- Durability (6 months)?
- All mAbs combinations provide similar duration of coverage
- Safety comparable to small molecule antiretroviral PrEP agents

bnAB PrEP MIGHT provide another tool, avoid ART resistance, and serve as very long-acting HIV prevention
Antibody Combination for PrEP?

Panel of 208 HIV-1 strains

IC80 (µg/ml)

- >50
- 10.0-50.0
- 1.00-10.0
- 0.100-1.00
- 0.01-0.100
- 0.001-0.01
- <0.001
## bNab PrEP Products

<table>
<thead>
<tr>
<th>Study</th>
<th>Product(s)</th>
<th>Routes</th>
<th>Long-acting</th>
<th>Combination</th>
<th>Status</th>
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<tbody>
<tr>
<td>HVTN 703/HPTN 081 HVTN 704/HPTN 085</td>
<td>VRC01</td>
<td>IV</td>
<td></td>
<td></td>
<td>Completed</td>
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<tr>
<td>HVTN 127/HPTN 087</td>
<td>VRC07-523LS</td>
<td>IV, SC, IM</td>
<td>√</td>
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<td>Manuscript in progress</td>
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<tr>
<td>HVTN 130/HPTN 089</td>
<td>PGT121, PGDM1400 10-1074, VRC07-523LS</td>
<td>IV</td>
<td>√</td>
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<td>HVTN 136/HPTN 092</td>
<td>PGT121.414.LS, VRC07-523LS</td>
<td>IV, SC</td>
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<td>PGDM1400LS, VRC07-523LS, PGT121.414.LS</td>
<td>IV, SC (?)</td>
<td>√</td>
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<td>IV, SC (?)</td>
<td>√</td>
<td>√</td>
<td>Protocol in development</td>
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Background and rationale:
As the global community works to extricate itself from the COVID pandemic, the HIV pandemic enters its 40th year. In the last 40 years, great strides have been made in HIV prevention, treatment and cure. Yet, considerable gaps remain in each of these realms—and have widened during the COVID pandemic—as evidenced by ongoing HIV incidence in the face of persistent challenges with ART initiation and adherence (1-3) and limited success with curative strategies, thus far (4-6). Broadly neutralizing antibodies (bnAbs) have the potential to fill gaps in all of these areas, and analytical treatment interruption trial designs facilitate simultaneous exploration of bnAbs’ potential for prevention, treatment and cure.
Multi-Purpose Technologies

Source: Adapted from Initiative for Multipurpose Prevention Technologies
Women want MPTs

83% of women prefer HIV/STI prevention products with contraception vs. HIV/STI prevention alone

The study product for the co-formulated MPT tablet will be provided in blister packs containing 21 tabs of emtricitabine, tenofovir disoproxil fumarate, levonorgestrel, and ethinyl estradiol (200 mg/300mg/0.15 mg/0.03 mg) + 7 tabs of emtricitabine, tenofovir disoproxil fumarate (200 mg/300mg).
Potentially a 2- to 10-fold increase in PrEP usage

Estimated DPP users compared to current PrEP users

- Current PrEP users (women and men)
- Estimated DPP users

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<th>Low range conversion estimate</th>
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<th>High range conversion estimate</th>
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<td>113,000</td>
<td>513,000</td>
<td>1,252,000</td>
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<tr>
<td>250,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>113,000</td>
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Achieving Population Impact

Integrated Strategies

Behavioral Interventions

Biomedical Interventions

Structural Interventions
HPTN 091: Study Design

169 participants enrolled
Comparing the efficacy of “one stop” integrated health services prevention in a mobile unit (Intervention): medication for opioid use disorder (MOUD), ART or PrEP, STI test and treat, harm reduction supplies – including naloxone kits plus peer navigation to an active control arm that receives peer navigation to integrated health services in the community for people who inject opioids living with HIV or at risk

174 participants enrolled
Getting to Zero in Black MSM in the American South (HPTN 096)

Pilot communities activated!
How Does The Integrated Strategy Work?

Community-Level Integrated Strategy

Intersectional Stigma Reduction

Peer Support

Social Media Influencers

Health Equity

HIV-

Increased HIV Testing

HIV+

Increased PrEP Uptake & Adherence

Increased ART Uptake & Adherence

Increase in Black MSM who are protected from HIV infection

Increase in Black MSM who are virally suppressed

Community-Level Outcomes
Community Engagement is pivotal part of all HPTN studies. Examples:

- Advocacy for affordable post-trial access to CAB LA in low- and middle-income countries where HPTN 083 and HPTN 084 being conducted
- Active in the development of forthcoming research initiatives (HPTN 102, 103, 104, and 106)
- Convened civil society consultation in preparation for implementation for HPTN 084 OLE
- Community led study branding for HPTN 096
HPTN Scholars Program

- 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
Meet the 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
Combination prevention for COVID-19

The coronavirus disease 2019 (COVID-19) pandemic has produced the fear and disorder inevitably provoked by emerging pathogens. As such, it should also inspire consideration of our experience with HIV over the past 40 years. As with HIV, the need to reduce infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the cause of COVID-19), and attendant morbidity and mortality, requires medical and nonmedical strategies. The most important lesson learned from tackling HIV is to use a combination of prevention strategies.

The first step to stopping the spread of SARS-CoV-2 has already been taken—behavioral changes. This reflects a rapid but imperfect understanding of the transmission of this virus. At the beginning of the AIDS epidemic, changes in sexual behavior, condom promotion, and government interventions (closing “hotspots” of HIV transmission such as bathhouses) made a difference. For SARS-CoV-2, masks and gloves, hand hygiene, and “shelter in place” mandates have already demonstrated benefits. More efficient behavioral intervention requires better understanding of the roles governing SARS-CoV-2 transmission. What are the risks from exposure to respiratory droplets, airborne virus, and surface contamination? What concentration of SARS-CoV-2 is required for transmission? Evidence suggests that SARS-CoV-2 transmission is greatest very early in infection prior to development of symptoms—the same lesson learned from HIV. Given this rule, medical prevention—like those described in this issue—will require large trials with multiple agents to improve success in eradicating the virus.

HIV has taught us that multiple concomitant prevention strategies are essential.

Myron S. Cohen & Lawrence Corey

Science. 2020 May 8;368(6491):551.
Beyond the Magic Bullet: What Will It Take to End the AIDS Epidemic?

Wafaa M. El-Sadr, MD, MPH, MPA

ABOUT THE AUTHOR

Wafaa M. El-Sadr is Global Director of ICAP at Columbia University, Mailman School of Public Health, Columbia University, New York, NY.

prevented the sexual transmission of HIV among heterosexual serodiscordant couples. Evidence soon followed of similar efficacy among gay men in serodiscordant partnerships. The recognition that treatment not only provides individual benefit but also prevents

FIGURE 1 — Integrated Strategies for HIV Prevention

Despite these advances, the successful prevention of HIV transmission requires a fundamental reconceptualization of the overall community's role. In this region, misperceptions regarding personal risk, competing life priorities, and difficulties in negotiating safer sex continue to pose threats to human health.

El-Sadr. AJPH, July 2021
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

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