HPTN MISSION

The HIV Prevention Trials Network (HPTN) advances HIV prevention through research:

• Develop integrated combination HIV prevention strategies

• Improve systemic pre-exposure prophylaxis (PrEP) and develop new PrEP agents and strategies

• Optimize application of new knowledge to key populations
The Year in Review: Metrics

- 9 ongoing studies including the HPTN 071 (PopART), the largest HIV prevention study to date
  - 6 new studies initiated/planned
- 78 sites are active (22 HPTN sites)
  - >25 new protocol-specific sites launched in the last year
- Successful scholars program
- 65 presentations, 47 publications
- Robust engagement of communities
- Expanded global partnerships
- 5 studies completed
We Are Building Partnerships

- Across Networks (VTN)
- BMGF
- VIIV, Gilead, Merck, and others (?)
- USAID
- The PANGEA Phylogeny Consortium
- The Northwestern Implant Consortium
- NIH Vaccine Research Center
The Effect of a Conditional Cash Transfer on HIV Incidence in Young Women in Rural South Africa (HPTN 068): a Phase 3, Randomised Controlled Trial

Audrey Pettifor, Catherine MacPhail, James P Hughes, Amanda Selin, Jing Wang, F Xavier Gómez-Olivé, Susan H Eshleman, Ryan G Wagner, Wonderful Mabuza, Nomhle Khoza, Chirayath Suchindran, Immitrude Mokoena, Rhian Twine, Philip Andrew, Ellen Townley, Oliver Laeyendecker, Yaw Agyei, Stephen Tollman, Kathleen Kahn

Phase 2 Study of the Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Men Who Have Sex With Men (HPTN 069/ACTG A5305)

HPTN 067/ADAPT key results presented:


• HPTN 067/ADAPT Study: A comparison of daily and non-daily pre-exposure prophylaxis dosing Thai/NYC. T. Holtz/S. Mannheimer et al. (IAS 2015)
HPTN 073
PrEP Uptake and Use by Black Men Who Have Sex With Men in Three U.S. Cities

Darrell P. Wheeler; Sheldon Fields; LaRon E. Nelson; Leo Wilton; Lisa Hightow-Weidman; Steven Shoptaw; Manya Magnus; Geetha Beauchamp; Phaedrea Watkins; Kenneth H. Mayer for the HPTN 073 Study
Antiretroviral Therapy for the Prevention of HIV-1 Transmission


UNAIDS Treatment Targets

- Diagnosed: 90%
- On Treatment: 90%
- Virally Suppressed: 90%
Treatment as Prevention Trials

- HPTN 071 (PopART)
- CDC Botswana
- ANRS Africa Center
- SEARCH Uganda

…and many smaller studies

PopART Intervention Package

- Annual rounds of home based voluntary HIV testing by Community HIV-care Providers (CHiPs)
- Health promotion, active referral and/or retention in care support by CHiPs for the following:
  - Voluntary Medical Male Circumcision (VMMC) for HIV negative men
  - Prevention of Mother to Child Transmission (PMTCT) for HIV positive women
  - HIV treatment and care for all HIV positive individuals
  - Promotion of sexual health and TB services
  - Condom provision
- ART irrespective of CD4-count or clinical stage provided at the local health centre

Population Cohort

- ~ 2,000 randomly selected adults (18-44) from each study community (N ~42,000)
- Annual household visits for blood collection and study survey completion for 3 years
- Study results will inform the primary outcome and some secondary outcomes

Primary Outcome: HIV Incidence
HPTN 074

Integrated intervention including supported ART compared to the standard of care for PWID

- Vietnam, Ukraine, Indonesia
- 504 HIV infected PWID
- 810 PWID “partners”
- Excellent retention
- Suppression results?
- Durability extension?
- What’s NEXT?
HPTN 078
Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected Men Who Have Sex with Men (MSM) in the United States

Study Design

Deep-Chain Respondent Driven Sampling (DC-RDS), and other methods

Screened population

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<tr>
<th></th>
<th>Enrolled participants</th>
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<tr>
<td>2700</td>
<td>356</td>
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<td>MSM &gt;= 16 yo</td>
<td>MSM HIV+, Unsuppressed</td>
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</table>

Study Duration: 24 M Follow-up

Enhanced Case Manager Intervention (n = 178)

SOC for Linkage and Treatment (n = 178)

Intervention

Control

Individual Randomization
There are approximately 1.2 million individuals in the United States living with HIV, with nearly 40,000 new cases diagnosed each year.\(^1,2\)

The Centers for Disease Control and Prevention estimated over 60% of new HIV infections in the United States were attributed to men who have sex with men (MSM), while 25% of new HIV infections occurred from heterosexual sex in 2010.\(^1\)

**CERTAIN POPULATIONS ARE AT HIGHER RISK OF CONTRACTING HIV THAN OTHERS**

The Centers for Disease Control and Prevention report these statistics estimating the number of people in the United States who will contract HIV in their lifetime.\(^3,4\)

<table>
<thead>
<tr>
<th>MEN WHO HAVE SEX WITH MEN (MSM)</th>
<th>MEN</th>
<th>WOMEN</th>
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<tbody>
<tr>
<td>Overall</td>
<td>1 in 6</td>
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<tr>
<td>African American</td>
<td>1 in 2</td>
<td>1 in 4</td>
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<tr>
<td>Hispanic/Latino</td>
<td>1 in 4</td>
<td>1 in 11</td>
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<tr>
<td>Caucasian</td>
<td>1 in 11</td>
<td>1 in 880</td>
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<tr>
<th>HETEROSEXUAL</th>
<th>MEN</th>
<th>WOMEN</th>
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<tbody>
<tr>
<td>Overall</td>
<td>1 in 473</td>
<td>1 in 241</td>
</tr>
<tr>
<td>African American</td>
<td>1 in 64</td>
<td>1 in 227</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>1 in 48</td>
<td>1 in 48</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 in 132</td>
<td>1 in 227</td>
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<tr>
<td>Injection Drug Users</td>
<td>1 in 36</td>
<td>1 in 23</td>
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**THE TRANSGENDER COMMUNITY IN THE UNITED STATES IS ONE OF THE HIGHEST-RISK GROUPS FOR HIV INFECTION**

HIV prevalence in transgender women was estimated at nearly 50 times higher than in all adults of reproductive age.\(^6\)

For more information, visit PreventHIV.com
Optimize the use of TDF/FTC

- Pharmacology and adherence (HPTN 066, 067)
- Vanguard (pilot) studies directed toward:
  - Acceptability in MSM in the US (HPTN 073)
  - Recruitment of MSM in Africa (HPTN 075)
  - PrEP uptake in women in Africa (HPTN 082)

Develop new PrEP/ drugs/delivery methods for PrEP

- Long-acting ART (HPTN 076, 077, 083, 084)
- Broadly neutralizing antibodies (HPTN 081, 085)
Primary objectives:
- Assess the proportion and characteristics women who accept versus decline PrEP
- Assess PrEP adherence using drug levels in young women

PrEP = Daily oral FTC/TDF

Enrolled participants

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<tr>
<td>229</td>
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## HPTN 083: CAB LA 600mg

To Prevent HIV Acquisition in MSM and TGW

Landovitz and Grinsztejn, Protocol Chairs

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Daily oral CAB and TDF/FTC placebo</th>
<th>TDF/FTC and oral CAB placebo</th>
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<tbody>
<tr>
<td></td>
<td>CAB LA at two time points 4 weeks apart and every 8 weeks thereafter and TDF/FTC placebo</td>
<td>TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
</tr>
<tr>
<td>Step 2</td>
<td>Open-label TDF/FTC to cover the PK tail</td>
<td>Open-label TDF/FTC to Cover the PK tail</td>
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**Primary Objective:** Reduce HIV Incidence (*non-inferiority*, double blind, double dummy design)

N=4500; Study duration: Enrollment 24-30 months; follow-up ~ 4.5 years

Enrollment goals:
- *Minimum* 50% of US enrollment Black MSM (~ 950)
- Overall minimum 10% TGW (~ 450)
- Overall > 50% under age 30
HPTN 083 Research Sites
44 Sites in 7 Countries

Study started in December 2016 in U.S.
122 Enrolled! (as of April 5 2017)
HPTN 084: CAB LA 600mg

To Prevent HIV Acquisition in Women
Delaney-Moretlwe and Hosseinipour, *Protocol Chairs*

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Daily oral CAB and TDF/FTC placebo</th>
<th>Oral TDF/FTC and oral CAB placebo</th>
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</thead>
<tbody>
<tr>
<td>CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
<td>Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter</td>
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<table>
<thead>
<tr>
<th>Step 2</th>
<th>Open-label oral TDF/FTC to cover the PK tail</th>
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<td>Open-label oral TDF/FTC to cover the PK tail</td>
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<tr>
<th>Step 3</th>
<th>Open-label oral TDF/FTC to cover the PK tail</th>
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<tr>
<td>Open-label oral TDF/FTC to cover the PK tail</td>
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</table>

**Primary Objective:** Reduce HIV Incidence (*superiority*, double blind, double dummy design)
Study duration: Enrollment 24 months; follow-up up to 4.5 years, N=3200
HPTN 084 Research Sites
(to date)
Subcutaneous PrEP Implants?
Like Implanon/Nexplanon Contraception

- Simple insertion AND removal
- Long-acting (months to years)
- PrEP + contraception?
- Current development:
  - TAF, EFdA (MK-8591), Cabotegravir

Partnerships established!
Phase 1 2019

Northwestern Medicine scientists have received a 5-year, $17.5 million grant from the National Institutes of Health (NIH) for an interdisciplinary project that aims to invent, develop and test an implantable drug delivery system to protect high-risk individuals from HIV infection for up to a year at a time.

The Sustained Long-Acting Protection Against HIV (SLAP HIV) program, funded by the NIH’s National Institute of Allergy and Infectious Diseases (NIAID), will bring together 15 basic scientists and clinical investigators from 15 departments across Northwestern University Feinberg School of Medicine, McCormick School of Engineering and Kellogg School of Management.
Sustained Long-Acting Protection Against HIV

SLAP-HIV
- Northwestern University

Patrick Kiser and Tom Hope
Neutralizing Ab to HIV-1

- V1V2-Glycan – binds to trimer cap
- V3-glycan, N332 supersite
- gp41 MPER – near membrane
- gp120/41 interface – bind to parts of both gp120 and gp41
- CD4 binding site of gp120 – where the virus attaches to CD4

Antibodies (VRC01, 3BNC117) and others in early phase clinical trials
The AMP Studies: Highlights

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<tr>
<th>Cohort</th>
<th>IV Treatment</th>
<th>n=</th>
<th>Schedule</th>
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<tbody>
<tr>
<td>North + South American MSM (2400)</td>
<td>VRC01 10 mg/kg</td>
<td>800</td>
<td>Every 8 wks x 10 doses</td>
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<tr>
<td></td>
<td>VRC01 30 mg/kg</td>
<td>800</td>
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<td>Placebo Control</td>
<td>800</td>
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<td>HVTN 704 / HPTN 085</td>
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<tr>
<td>sub-Saharan African women (1500)</td>
<td>VRC01 10 mg/kg</td>
<td>500</td>
<td>Every 8 wks x 10 doses</td>
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<tr>
<td></td>
<td>VRC01 30 mg/kg</td>
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<td>Placebo Control</td>
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<tr>
<td>HVTN 703 / HPTN 081</td>
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- Two different infusion doses: important to know if lower dose of 10 mg/kg can protect
- Powered to associate mAb serum level with protection
- All subjects provided an HIV “prevention package”
AMP Research Sites
47 sites in 11 countries

HVTN 704/HPTN 085, MSM + TG
HVTN 703/HPTN 081, Women
AMP Enrollment Update
As of April 6, 2017

703/081 African Women
557/1500 enrolled

704/085 MSM + TG
978/2700 enrolled
HPTN Scholars Program

Goal: To develop the next generation of HIV prevention scientists from under-represented racial/ethnic communities

- Scholars utilize HPTN data to develop analytic skills, conduct reviews, give presentations, write publications

To date: - 26 scholars completed program
- 31 mentors engaged
- K & U awards, R01, R03s, R21s, faculty positions
- 18 publications
  (+ 2 in press, 1 under review)
Community Engagement Activities

- **Good Participatory Process**
  - Five HPTN 083 presentations at national conferences engaging community advocates, CBOs, ASOs, MSM & TG-specific service providers, and health departments
  - One HPTN 083 community webinar engaging U.S. national community advocates and providers

- **Scientific Literacy**
  - “Understanding Clinical Research Process and Principles of Clinical Research” workshop for the HPTN 071/PopART Zambia National CAB

- **Community partnerships**
  - Five, study-specific national stakeholder consultations

- **Social Media**
  - #GivePrEPaShot social marketing campaign and website for HPTN 083

- **Dissemination of Results**
  - Webinars, at sites, brochures, etc.
Cross Site Exchange of Best Practices
Building on Lessons Learned in the Community
Community Outreach/Education
Implementing Community Engagement for Combination Prevention: Lessons Learnt From the First Year of the HPTN 071 (PopART) Community-Randomized Study

Musonda Simwanga¹ · Virginia Bond¹,³ · Nozizwe Makola² · Graeme Hoddinott² · Steve Belemu¹ · Rhonda White⁴ · Kwame Shanaube¹ · Janet Seeley³,⁵ · Ayana Moore⁴ · on behalf of the HPTN 071 (PopART) study team
HPTN 083 “Give PrEP a Shot” website, social marketing, and materials
Dissemination - Cross Network Collaboration

The AMP Studies: Antibody-Mediated Prevention

These are landmark studies to establish whether IV infusions of VRC01, a broadly neutralising antibody produced in the laboratory, will protect HIV-negative individuals against infection, and what dose is needed to achieve protection.

The AMP Studies will enroll:
- 2,700 men and transgender people who have sex with men at 25 sites in North and South America and Europe
- 1,500 heterosexual women at 15 sites in sub-Saharan Africa

HPTN 083: Long-Acting Injectable PrEP

HPTN 083 is a safety and efficacy research study designed to test if the injectable ARV cabotegravir, administered once every eight weeks, will prevent HIV infection as well as daily oral Truvada in men who have sex with men and transgender women.

It will enroll 4,500 participants at research sites in Argentina, Brazil, Peru, South Africa, India, Thailand, Vietnam and the US.

PLEASE JOIN US FOR AN EXCITING BREAKFAST PLenary AT THE 2017 NAESM MEETING!

Saturday, January 21, 8:30-10 a.m. • Bent Tree 1-2
Dallas/Addison Marriott Quorum by the Galleria • Dallas, Texas

HIV Prevention Research Studies Engaging Black MSM and Transgender Persons

Presenters will provide updates on two biomedical HIV prevention research studies that seek to advance HIV prevention options available for Black MSM, and transgender men and women who have sex with men, with the ultimate goal of reducing the HIV epidemic among these groups.
Dissemination – Best Practices
# HPTN Research Portfolio Timeline

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<tr>
<td>HPTN 071</td>
<td>POPART (Phase 3)</td>
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<td>HPTN 074</td>
<td>ART for Prevention, PWID (Vanguard)</td>
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<td>HPTN 075</td>
<td>MSM Sub Saharan Africa (Vanguard)</td>
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<tr>
<td>HPTN 078</td>
<td>Enhanced recruitment, linkage, care and treatment in US MSM (Vanguard)</td>
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<td>HPTN 082</td>
<td>PrEP Young African Women (Vanguard)</td>
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<td>HPTN 076</td>
<td>Injectable TMC278LA for PrEP (Phase 2)</td>
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<td>HPTN 077</td>
<td>Injectable Cabotegravir for PrEP (Phase 2)</td>
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<tr>
<td>HPTN 083</td>
<td>Injectable Cabotegravir for PrEP_MSM (Phase 2b/3)</td>
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<td>HPTN 084</td>
<td>Injectable Cabotegravir for PrEP_South African Women</td>
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<td>HVTN 703/</td>
<td>AMP Women (Phase 2b)</td>
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**Study Development to Anticipated Last F/U Visit**

- PrEP Implant Phase 1 study
- PreP Implant Phase 2/3 studies
- Combination monoclonals
The Way Forward

When we complete our current studies we will have:

• A long-acting PrEP agent ready for licensing as an alternative prevention product, if proven successful.
• Determined strategies to deliver HIV testing and universal access to ART to decreases HIV incidence
• Established methods for optimizing uptake of TDF/FTC in MSM in the U.S. and young women in Africa
• Advanced BnABS for prevention of HIV infection and

THE BIG PICTURE: HPTN IS DETERMINED TO GENERATE RESEARCH RESULTS THAT INFORM AND GUIDE HIV PREVENTION STRATEGIES WORLDWIDE
Acknowledgements

• NIH Institutes (NIAID, NIMH, NIDA) and OAR

• HPTN Scientific Committees, Working Groups, Executive Committee and the Scientific Advisory Group

• Study participants and participating communities

• Site investigators, staff, and community representatives

• BMGF, USAID, PEPFAR/OGAC, ViiV, Gilead and others