HPTN 2017-8
The Way Forward
Myron S. Cohen
Wafaa El-Sadr
on behalf of the HPTN
The HIV Prevention Trials Network (HPTN) advances HIV prevention through research:

- Integrated HIV prevention strategies
- Improve pre-exposure prophylaxis (PrEP)
- New strategies for key populations
What Does this Really Mean?

- We are trying to develop tools/strategies
  - That improve public health policy/practice
  - That improve medical care
  - In a timely fashion (FAST)
Highlights

• Where have we been?
• Where are we going?
• **WE NEED YOU (!!!) to go anywhere**
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
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)

Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial

Prof Linda-Gail Bekker, MD, Surita Roux, MBChB, Elaine Sebastien, RNRM, Ntando Yola, PgDPh, K Rivet Amico, PhD, Prof James P Hughes, PhD, Mark A Marzinke, PhD, Craig W Hendrix, MD, Prof Peter L Anderson, PharmD, Vanessa Elharrar, MD, Michael Stirratt, PhD, James F Rooney, MD, Estelle Piwowar-Manning, MT(ASCP), Prof Susan H Eshleman, MD, Laura McKinstry, MPH, Maoji Li, MMath, Bonnie J Dye, MPH, Robert M Grant, MD, on behalf of the HPTN 067 (ADAPT) study team
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.\(^3,4\)

### MEN WHO HAVE SEX WITH MEN (MSM)

<table>
<thead>
<tr>
<th></th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1 in 6</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>1 in 2</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>1 in 4</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 in 11</td>
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</tbody>
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**HETEROSEXUAL**

<table>
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<tr>
<th></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 227</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 in 132</td>
<td>1 in 880</td>
</tr>
<tr>
<td>Injection Drug Users</td>
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**OVERALL**

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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.\(^4\)

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**For more information, visit PreventHIV.com**
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
MSM: HPTN 075 and 078

Studies designed to better inform our ability to prevent HIV in hard to reach MSM …worldwide
HPTN 076: TMC278 LA Safe, Tolerable, And Acceptable for HIV Pre-exposure Prophylaxis

Linda-Gail Bekker, Shuying S. Li, Betsy Tolley, Mark A. Marzinke, Nyaradzo Mgodi, Jessica E. Justman, Shobha Swaminathan, Adeola Adeyeye, Jennifer H. Farrior, Nirupama Sista

HPTN 076: Safety and Pharmacokinetics of Rilpivirine LA Through Week 76 in HIV-uninfected Women

Diagnosed: 90%
On Treatment: 90%
Virally Suppressed: 90%

UNAIDS 2014
HPTN 052

Bruce Alberts, Editor of Science explains the choice of this work:

“The results have galvanized efforts to end the world’s AIDS epidemic in a way that would been inconceivable even a year ago”
Treatment as Prevention Trials

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

...and many smaller studies

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?
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, 086)
- Broadly neutralizing antibodies (HPTN 081, 085, 087, 088)
HPTN 082 Study Design

Standard Adherence Support

- CBT counseling, SMS texting, Adherence clubs

Enhanced Adherence Support

- Standard plus drug level feedback counseling

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

229
**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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<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></td>
<td></td>
</tr>
<tr>
<td>Step 3</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.
651 Enrolled! (as of October 12 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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**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
Study Population

- 20 research sites in 7 countries in Sub-Saharan Africa
- 3,200 women who have sex with men
- Expected HIV incidence >3/100 person years
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

Passive Antibody Prevention
Phase IIB Efficacy Studies

Can a passively infused monoclonal antibody prevent HIV-1 infection in high risk adults: MSM in Americas & Heterosexual Women in sub-Saharan Africa?

AMP = Antibody Mediated Prevention

Chairs: Lawrence Corey, HVTN
Myron S. Cohen, HPTN

Co-chairs: Srilatha Edupuganti
Nyaradzo Mgodi
The AMP Studies: Highlights
HVTN 704/HPTN 085
HVTN 703/HPTN 081

• Placebo controlled trial of VRC01 mAb (IV), given on q2 month schedule

• Two cohorts:
  - 2,400 MSM + TG in North & South America
  - 1,500 Women in sub-Saharan Africa

• Powered to detect 60% efficacy; and to associate VRC01 plasma level with protection

• Both trials opened in April/May 2016
AMP Research Sites

47 sites in 11 countries
AMP Enrollment Update
As of October 12, 2017

703/081
African Women
1213/1500 enrolled

704/085
MSM + TG
1748/2700 enrolled
Broadly neutralizing antibodies to prevent HIV-1

Studies show the potential of synthetic and Combinations of broadly neutralizing antibodies.

By Myron S. Cohen and Lawrence Corey
bnAbs prevent HIV-1

Combinations of bnAbs and a trispecific antibody can bind to virions and prevent HIV-1 mucosal infection and elicit antiviral responses in deeper tissue. It is hoped this multitarget approach will prevent resistant breakthrough.

bnAbs in epithelial mucosa
A mixture of two bnAbs, PGDM1400 and PGT121, or a trispecific bnAb prevent infection of CD4 T cells from HIV-1.

bnAbs in deeper tissue
bnAbs can also protect tissues from HIV-1 infection through natural killer cells or other phagocytic cells, with no latent or persistent viral replication in lymphoid tissue.
HPTN Scholars Program

**Goal:** To develop the next generation of HIV prevention scientists from underrepresented 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
Community Engagement Activities

- **Community partnerships**
  - Five, study-specific national stakeholder consultations (including HPTN 081 and HPTN 084)
  - SA AIDS booth, photo campaigns

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

- **Dissemination of Results**
  - Webinars, at sites, brochures, posters, presentations, etc.
Cross Site Exchange of Best Practices
Community Outreach/Education
Community Outreach/Education

**084: LONG-ACTING INJECTABLE PrEP**

084 is a safety and efficacy research study designed to test if an injectable ARV cabotegravir, given once every 2 weeks, will prevent HIV infection better than daily tenofovir disoproxil fumarate and emtricitabine (Truvada) in women at high risk of acquiring HIV. The study included 2,200 participants at sites in Botswana, South Africa, Swaziland, Zambia, and Zimbabwe.
Dissemination - Cross Network Collaboration

The AMP Studies: Antibody-Mediated Prevention

These are landmark studies to establish whether IV infusions of VIRGO, 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 enrol:
- 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, given subcutaneously 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 enrol 3,500 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
Women and Adolescent Subjects

- ~40,000 women in HPTN clinical trials
- A rapidly growing and exciting adolescent research agenda team
- Consideration of ethical bridging studies
The Way Forward

When we complete our current studies we will have:

- A long-acting PrEP agent
- Strategies to deliver HIV testing and universal access to ART to decrease HIV incidence
- Methods for optimizing uptake of TDF/FTC
- Advanced BnABS for prevention of HIV infection

THE HPTN IS DETERMINED TO GENERATE RESEARCH RESULTS THAT INFORM AND GUIDE HIV PREVENTION STRATEGIES WORLDWIDE
The Team

• Study participants and participating communities
• Site investigators, staff, and community representatives
• BMGF, USAID, PEPFAR/OGAC, ViiV, Gilead, VRC, PANGEA, and many other partners
• NIH Institutes (NIAID, NIMH, NIDA) and OAR
• HPTN Scientific Committees, Working Groups, Executive Committee, and Scientific Advisory Group