HIV Prevention Network (HPTN)
State of the Network

Wafaa El-Sadr, MD, MPH, MPA
May 2013
Washington, DC
Change in HIV Incidence

- Increasing >25%
- Stable
- Decreasing >25%
- Not included in analysis

UNAIDS, 2010
2.5 million people infected every year
<table>
<thead>
<tr>
<th>Biomedical</th>
<th>Behavioral</th>
<th>Structural</th>
<th>Integrated Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPTN 052</td>
<td>HPTN 061*</td>
<td>HPTN 043*</td>
<td>HPTN 065</td>
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<tr>
<td>HPTN 058*</td>
<td>HPTN 062*</td>
<td>HPTN 068</td>
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<td>HPTN 066</td>
<td>HPTN 063</td>
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<td>HPTN 067</td>
<td>HPTN 064*</td>
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<td>HPTN 069</td>
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<td>HPTN 073</td>
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<tr>
<td>HPTN 076@</td>
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* completed
@ in development
<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Status</td>
<td>HIV negative, acute infection, established HIV infection</td>
</tr>
<tr>
<td>Populations</td>
<td>Adolescents, MSM, women, IDU, communities</td>
</tr>
<tr>
<td>Interventions</td>
<td>Behavioral, HIV testing, PrEP, ART, VMMC, substitution/antagonist therapy, financial incentives, integrated strategies</td>
</tr>
<tr>
<td>Types of Studies</td>
<td>Observational, individual randomized, site randomized, community randomized, implementation science</td>
</tr>
</tbody>
</table>
Prevention for HIV+ and HIV-Persons

- **TEST**
  - **Positive**
    - Engage, Counsel, Monitor and Support
    - **HIV CARE (Pre-ART)**
    - Retain, Counsel, Monitor, and Support
    - Adherence and Viral Suppression
  - **Negative**
    - Engage, Counsel, Monitor and Support
    - **Pre-Exposure Prophylaxis (PrEP), Male Circumcision, Condoms**
    - Counsel, Intervene, Monitor, and Support
    - Support Adherence, Monitor, Repeat HIV Testing
Project Accept
(HPTN 043)
Increase in knowledge of HIV status in a community will be associated with decreased HIV incidence
Communities randomized to two approaches
Mobilization, Testing, Support, and Access to Services

• Community-based VCT (CBVCT N = 24 communities)
  • Community preparation, outreach, mobilization
  • Mobile VCT
  • Post-test support services
    – Stigma-reduction skills training
    – Coping effectiveness training
    – Ongoing counseling
  • Ongoing data feedback and field adjustments

• Standard VCT (SVCT N = 24 communities)
  • Clinic-based VCT
  • Standard VCT services normally provided in that community

Van Rooyen et al, AIDS and Behavior, 2012
86,720 HIV tests

69,987 in CBVCT communities

7,636 in SVCT communities

50,000 individuals when repeat tests are excluded

140,755 post-test support visits

Sweat et al, Lancet ID, 2011
Primary outcome: HIV incidence, evaluated at the *community* level

- The goal was to affect the entire community and *not just a study cohort*

- Outcomes evaluated at the end of the intervention among a probability sample of *54,326 community residents* 18 to 32 years of age

- Incident rates were estimated using a multi-assay algorithm
Cross-sectional HIV incidence estimation

- CD4 cell count
  - > 200
  - BED CEIA
    - < 1.0
    - Avidity
      - < 80%
      - HIV viral load
        - > 400
        - Recent / incident Infection

Graph:
- Annual HIV Incidence (%)
- Longitudinal (cohort)
- Cross-sectional (MAA)

Alternate testing algorithms for clade B / US
- No need for CD4 cell count data
- Use of a novel HIV diversity assay

Optimized methods for HIV incidence estimation in Project ACCEPT (HPTN 043)
## Incidence Differences: Intervention versus Control Communities

<table>
<thead>
<tr>
<th>Subgroup (N of Incident Infections)</th>
<th>Effect&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants (464)</td>
<td>0.86</td>
<td>0.73 – 1.02</td>
<td>0.0822</td>
</tr>
<tr>
<td>Women (316)</td>
<td>0.88</td>
<td>0.73 – 1.06</td>
<td>0.1691</td>
</tr>
<tr>
<td>Men (148)</td>
<td>0.81</td>
<td>0.57 – 1.15</td>
<td>0.1934</td>
</tr>
<tr>
<td>Age 18-24 years (271)</td>
<td>0.98</td>
<td>0.80 – 1.22</td>
<td>0.8554</td>
</tr>
<tr>
<td>Age 25-32 years (193)</td>
<td>0.75</td>
<td>0.54 – 1.04</td>
<td>0.0777</td>
</tr>
<tr>
<td>Women, age 18-24 years (201)</td>
<td>1.00</td>
<td>0.78 – 1.28</td>
<td>0.9833</td>
</tr>
<tr>
<td>Women, age 25-32 years (115)</td>
<td>0.70</td>
<td>0.54 – 0.90</td>
<td>0.0085</td>
</tr>
<tr>
<td>Men, age 18-24 years (69)</td>
<td>0.95</td>
<td>0.64 – 1.40</td>
<td>0.6934</td>
</tr>
<tr>
<td>Men, age 25-32 years (79)</td>
<td>0.78</td>
<td>0.41 – 1.47</td>
<td>0.3914</td>
</tr>
</tbody>
</table>

<sup>a</sup> Relative risk of infection (CBVCT vs. SVCT); weighted incidence ratio
• An almost 4-fold increase in the detection of previously undiagnosed HIV cases

• Increase in HIV testing by 45% among men and 15% among women

• Number of sexual partners reported by HIV-infected individuals significantly lower by 8% 95% CI: 1% - 15%, p = 0.03

• Number of sexual partners among HIV-infected men significantly lower by 18% 95% CI: 5% to 28%, p = 0.009

• Multiple sexual partners significantly lower by 30% 95% CI: 0.54 – 0.92, p = 0.01

• Multiple sexual partners among HIV-infected men significantly lower by 29% 95% CI: 0.57 to 0.89, p = 0.0006

Sweat et al, Lancet ID, 2011
HIV Treatment for Prevention: HPTN 052

The New York Times

EDITORIAL
When Treatment Is Also Prevention
Published: May 22, 2011

The discovery of a near-perfect way to halt sexual transmission of the AIDS virus has the potential for quick and nations cope with troubling issues of cost.

The end of AIDS?

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D., Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D., Smita Mahendraker, M.D., Sayantani Ghoshal, M.D., Bruce R. Scatter, M.D., Kenneth H. Mayer, M.D.
HPTN 052 Study

1,763 sero-discordant couples (97% heterosexual) HIV infected partners: 890 men, 873 women

39 HIV Transmissions

- 28 linked HIV transmissions
- 11 unlinked

Immediate ART:
- 1 transmission

Deferred ART:
- 27 transmissions

☑️ 96% Protection
Phylogenetic Analysis

Transmission linkage
Transmission dynamics
Co-infection / Super-infection
ART for Prevention

Test

- Testing
- HIV Positive
- Positive Prevention
- Adopt safer behaviors

Enroll in Care

- Initiation of ART
- Treat
- Adherence to ART
- Maintain viral suppression

Linkage to care

Decrease in HIV Transmission
HPTN 065
Test Link to Care Plus Treat (TLC-Plus)
PURPOSE

To evaluate the feasibility of an enhanced community-level HIV test, link-to-care plus treat strategy in the U.S.
Behavioral Economics

37 testing sites

39 care sites

CARD

CARD
**HPTN 065 Study Design**

### HIV Testing & Linkage to Care
- **Expand HIV Testing**
  - Social Mobilization
  - Universal offer of testing in ED/hospital admission

- **HIV Testing Sites**
  - 38 Randomized HIV Test Sites to link HIV positives
  - Financial incentive plus SOC
  - Standard of care (SOC)

### HIV Treatment
- **HIV Care Sites**
  - 39 Randomized HIV Care Sites
  - Financial incentive plus SOC
  - Standard of care (SOC)

### Prevention for Positives
- **Select HIV Care Sites**
  - Individual randomization of 660 patients in 2 communities
  - CARE plus Standard of Care
  - Standard of Care
Intersection Between Surveillance and Research

Partnership with CDC and Departments of Health

- HIV Surveillance data to monitor US care cascade for HPTN 065 (linkage and viral suppression)

- DOH data from New York, Washington DC, Chicago, Miami Philadelphia and Houston

- Strengthening HIV surveillance data through novel public health research
HPTN 065: Timeline

- Expanded HIV Testing
  - Social Mobilization
    - Linkage-to-Care & Viral Suppression
      - Prevention for Positives

2010 2011 2012 2013 2014 2015

* Provider Surveys
* Patient Surveys (part of PfP)
HPTN 071
(PopART Study)
HPTN 071 (PopART)

Hypothesis

Integrated strategy of

- Universal voluntary HIV testing
- Appropriate combination prevention offered to all those testing HIV negative
- Immediate ART for all those testing HIV positive

will have a substantial impact on HIV incidence at population level
- 12 communities in Zambia
- 9 communities in the Western Cape of South Africa
- Total study population of 1.2 million persons
Primary Objective

- To measure the impact of the PopART intervention in reducing HIV incidence

- HIV incidence to be measured in a cohort of **52,500** adults over 3 years
Every minute, a young woman is newly infected with HIV.

As a result of their lower economic, socio-cultural status in many countries, women and girls are disadvantaged when it comes to negotiating safe sex, accessing HIV prevention information and services.

11-45% of adolescent girls report that first sexual experience was forced.

Women living with HIV are more likely to experience violations of their sexual and reproductive rights, for example forced sterilization.

2x
Globally, young women aged 15-24 are most vulnerable to HIV, at a rate twice as high as in young men, and accounting for 22% of all new HIV infections.

Only once condition is available for every 30 women in Sub-Saharan Africa.

Women may find it hard to access care if they hide their HIV status.

Most women (60%) of women aged 20-24 years in the developing world marry before they are 18 years old.

40%
Approximately 40 percent of programmes worldwide are unresponsive to the needs of young women and girls.

Globally, less than 30% of young women have comprehensive knowledge on HIV.

32/94
Women living with HIV are not regularly involved in formal processes to plan and review the national HIV responses to AIDS in 22 of 94 countries.

Sources:
1. UNAIDS, 2013
2. UNAIDS, 2013
3. UNAIDS, 2013
4. UNAIDS, 2013
5. UNAIDS, 2013
6. UNAIDS, 2013
7. UNAIDS, 2013
8. UNAIDS, 2013

S. Delaney-Morotlwe, CROI 2013
3.9 million young people in Sub-Saharan Africa aged 15 – 24 years are living with HIV. Three-quarters are young women.
HPTN 068: Effects of Cash Transfer for the Prevention of HIV in Young South African Women
Does providing cash transfers to young women and their household, conditional on school attendance, reduce structural barriers to education and thereby reduce young women’s risk of acquiring HIV?
HPTN 068 Study Design

- A Phase III individually randomized design
- A total of 2,536 young women were randomized (enrollment complete)
- South Africa
HPTN 068 Study Groups

• Structural Intervention Arm
  – Young woman and her parents receive monthly cash transfer payments conditional on the young woman’s school attendance (must be ≥ 80% of in-session days)

• Control Arm
  – No payments given to the participant
• Men who have sex with men (MSM) represent 2% of the US population, yet are the most severely affected
• In 2011 MSM accounted for
  – 62% of all new HIV infections
• Black/African American MSM (BMSM) accounted for 38% of new HIV infections in 2011
• HIV infection rates increased 48% from 2006–2009 among young BMSM aged 13–29
• 1,553 Black MSM enrolled

• Annual HIV incidence 3.0% (CI: 2.0-4.4%)
  
  – HIV annual incidence of 5.9% in men ≤30 years of age (CI: 3.6-9.1%)
HPTN 073

Pre-Exposure Prophylaxis (PrEP) Initiation and Adherence among Black Men Who Have Sex with Men (BMSM)
To assess the initiation, acceptability, safety, and feasibility of PrEP for Black men who have sex with men (BMSM) utilizing client-centered care coordination (C4) models
Study Design

• An open label observational study

• 225 HIV-uninfected BMSM at risk for HIV infection in three U.S. cities

• Once daily oral emtricitabine 200 mg / tenofovir 300 mg (FTC/TDF) with Client-Centered Care Coordination (C4)

• A subset of men will participate in qualitative interviews about facilitators and barriers regarding PrEP
Primary Objectives

• To assess the initiation and correlates of daily PrEP use by sociodemographics, including age, education, and risk practices

• To assess PrEP adherence via self-report (ACASI) and antiretroviral drug detection
• Rapid, low cost ARV drug screening
• Simultaneous detection of other drugs / substances
• Adherence monitoring
• Undisclosed (off-study) ARV drug use

**HPTN 052**
“ARV naïve”

<table>
<thead>
<tr>
<th>Enrollment VL (c/ml)</th>
<th>% ARVs Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;400</td>
<td>46.9% 45/96</td>
</tr>
<tr>
<td>401-1000</td>
<td>4.2% 2/48</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>1.5% 1/65</td>
</tr>
</tbody>
</table>

**HPTN 061**
“Newly Diagnosed”

<table>
<thead>
<tr>
<th>Enrollment VL (c/ml)</th>
<th>% ARVs Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;400</td>
<td>92.6% 63/68</td>
</tr>
<tr>
<td>401-1000</td>
<td>53.3% 8/15</td>
</tr>
</tbody>
</table>
HPTN 066: PK for intermittent PrEP
HPTN 067: PK and behavioral study of intermittent PrEP in MSM and women
HPTN 069: Maraviroc for PrEP in MSM and women

HPTN 073: Uptake of PrEP by Black MSM
HPTN 076: Safety of injectable long acting TMC278LA in women
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Key Intervention</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPTN 066</td>
<td>32 HIV-uninfected, healthy, sexually-active men and women in the US</td>
<td>Oral TDF/FTC (Truvada®) – one or two tablets once or twice weekly, depending upon randomization arm</td>
<td>PK/PD</td>
</tr>
<tr>
<td>HPTN 067</td>
<td>540 participants including 180 women and 360 MSM/TGW and in SA, Thailand and the US respectively</td>
<td>Oral FTC/TDF (Truvada®) in three dosage groups: daily, time-driven, and event-driven</td>
<td>PK/PD and behavioral aspects</td>
</tr>
<tr>
<td>HPTN 069</td>
<td>400 MSM and 200 women across 12 sites in the US</td>
<td>Randomization to one of the following (once daily):</td>
<td>Safety, Tolerability, Adherence, PK/PD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. MVC + FTC placebo + TDF placebo</td>
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<tr>
<td></td>
<td></td>
<td>2. MVC + FTC + TDF placebo</td>
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<td></td>
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<td>3. MVC + TDF + FTC placebo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. TDF + FTC + MVC placebo</td>
<td></td>
</tr>
<tr>
<td>HPTN 073</td>
<td>225 HIV-uninfected BMSM in the US</td>
<td>Once daily TDF/FTC (Truvada®) + C4 (Client-Centered Care Coordination)</td>
<td>Acceptability, Adherence</td>
</tr>
<tr>
<td>HPTN 076</td>
<td>165 women in sub-saharan Africa and the US</td>
<td>TMC278 LA or placebo injections every 2 months</td>
<td>Safety, Tolerability, Acceptability</td>
</tr>
</tbody>
</table>
• Latino ethnicity, HIV risk correlates, and high-risk sexual behavior among HIV-negative Black MSM (HPTN 061)  
  Dr. Andres Bedoya

• Typologies of Testing: A Qualitative Analysis of HIV Testing Patterns Among Black MSM in Atlanta, GA (HPTN 061)  
  Dr. Sophia Hussen

• Tell me who your sex partners are and I will tell you who you are: A Comparison of Sexual Network Partners with Community-Recruited Participants from the HPTN 061 Project  
  Dr. Grace (Chela) Hall

• Racial/ethnic differences in injector networks & factors associated with membership in networks w/ HIV (HPTN 037)  
  Dr. Chevy Williams

• The Association Between Venues where Women at Risk of HIV Meet Sexual Partners and Partner HIV Risk Characteristics (HPTN 064)  
  Dr. Malika Roman Isler

• Attitudes and Believes about Individual and Community HIV/STI Risk among Women at Risk for HIV Acquisition in HPTN 064  
  Dr. Oni Blackstock

• Prevalence and HIV Risk-Related Correlates of Emotional, Physical, and Sexual Violence Among Women at Risk in the US (HPTN 064)  
  Dr. Brooke Montgomery
STATE OF THE ART
HIV PREVENTION

A JAIDS supplement sponsored by the HIV Prevention Trials Network (HPTN)

Guest Editors:
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David Serwadda, MD
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