HPTN 073: Black MSM Open-Label PrEP Demonstration Project
Overview

• HIV Epidemiology in the U.S.
• Overview of PrEP
• Overview of HPTN
• HPTN 061
• HPTN 073
• ARV Drug Resistance
• Conclusions
• Questions and Answers
HIV in the United States
Overview of the United States Epidemic

• More than 1.1 million people in the U.S. are living with HIV infection
• Almost 1 in 5 (18.1%) are unaware of their infection
• By race, Blacks/African Americans face the most severe burden
• Gay, bisexual, and other men who have sex with men (MSM), particularly young Black/African American MSM (BMSM), are most seriously affected
Estimated New HIV Infections in the United States and 6 Dependent Areas, 2011, for the Most Affected Subpopulations - CDC
HIV Among Blacks

• Experience the most disproportionate burden compared with other races and ethnicities

• Represent approximately 12% of the U.S. population, but accounted for 46% of new HIV infections in 2011

• Since the epidemic began, more than 260,800 Blacks with an AIDS diagnosis have died
HIV Among MSM

- MSM represent 2% of the US population, yet are the most severely affected.
- In 2011 MSM accounted for:
  - 62% of all new HIV infections
  - MSM-IDU accounted for an additional 3% of new infections
- BMSM accounted for 38% new HIV infections in 2011.
HIV Prevention Challenges for BMSM

- High HIV prevalence in the BMSM community
- Many unaware of HIV status
- Sexual risk behaviors
- Alcohol and illegal drug use near time to sex
- Internal and external homophobia, stigma and discrimination
Pre-Exposure Prophylaxis (PrEP) Background
Prior to PrEP ways to prevent getting HIV were:

– Abstaining from having sex,
– Having sex with only one person who is not infected with HIV and who agrees not to have sex with anyone else, and
– Using a condom correctly every time you have sex.

New ways to prevent getting HIV are urgently needed.

Recent research has shown that oral antiretroviral medications may prevent new HIV transmissions.
What is PrEP?

- PrEP (Pre-Exposure Prophylaxis) is a new approach that has shown that the use of antiretroviral medications (ARVs) can reduce the risk of HIV infection in HIV-negative people.
- In mid-2012 the FDA approved Truvada® to be used for as PrEP prevention of HIV.
- Used as part of a HIV prevention package (risk reduction counseling and condoms).
Why the Interest in PrEP?

• Data from numerous animal/human studies show protection from PrEP
• Antiretroviral therapy (ART) for prevention of mother to child transmission (PMTCT) provides proof of concept in humans
• Success of Post-Exposure Prophylaxis (PEP) for needle stick exposure in observational data
• Intermittent PrEP – administration of PrEP at irregular intervals – may reduce costs and exposure of negative individuals to ART
<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Study population</th>
<th>Design</th>
<th>Results: Reduction in HIV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PREP</td>
<td>4758 discordant couples in Kenya and Uganda</td>
<td>TDF (Viread) vs. TDF/FTC (Truvada®) vs. placebo</td>
<td>TDF: 67% TDF/FTC: 75% (86-90% if drug levels detectable)</td>
</tr>
<tr>
<td>CDC – TDF-2</td>
<td>1200 Adults in Botswana (45% women)</td>
<td>TDF/FTC (Truvada®) vs. placebo</td>
<td>TDF/FTC: 62%</td>
</tr>
<tr>
<td>iPrEx</td>
<td>2499 Gay Men in Brazil, Ecuador, Peru, South Africa, Thailand and the United States</td>
<td>TDF/FTC (Truvada®) vs. placebo</td>
<td>TDF/FTC: 44% (92% if drug levels detectable)</td>
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<tr>
<td>Study (reference)</td>
<td>Study population</td>
<td>Design</td>
<td>Results</td>
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<tr>
<td><strong>FEM-PrEP</strong></td>
<td>2120 Women in Kenya, South Africa and Tanzania</td>
<td>TDF/FTC (Truvada®) vs. placebo</td>
<td>Product not proven effective in preventing HIV due to low adherence (approximately 33% adherent)</td>
</tr>
<tr>
<td><strong>MTN-003 (VOICE)</strong></td>
<td>5,029 Women in South Africa, Uganda, and Zimbabwe</td>
<td>TDF (Viread) vs. placebo TDF/FTC (Truvada®) vs. placebo TDF gel vs. placebo</td>
<td>No product proven effective in preventing HIV due to low adherence (23%-29% adherent)</td>
</tr>
</tbody>
</table>
PrEP Adherence

- The level of protection depends on how consistently participants used PrEP.
- Greater levels of protection were found among those who adhered well to the daily dosing regimen.
- Other than low adherence, no factors have yet been identified that influence the effectiveness of PrEP.
PrEP Recommendations

• PrEP should be targeted to individuals at high risk for HIV infection
• PrEP should be taken as a daily medication consistently
• Women who are pregnant or trying to conceive should discuss potential risks and benefits of PrEP with a health care provider
• PrEP should be delivered as part of a comprehensive package of prevention services
• Individuals prescribed PrEP must be HIV negative
HIV Prevention Trials Network Overview
The HIV Prevention Trials Network (HPTN) is a partnership between scientists and communities around the world to develop, evaluate and implement cutting-edge biomedical, behavioral and structural interventions to reduce the transmission of HIV including PrEP, treatment as prevention and combination research.
HPTN’s Portfolio

- 80 research sites in 15 countries
- 50 clinical trials ongoing or completed
- 50,000 study participants followed
- 300 publications
HIV Prevention Tool Box

- Male Circumcision
- HIV Counseling and Testing
- Treatment for Prevention
- Treatment of STIs
- Behavioral Interventions
- Prevention for Positives
- Needle Exchange
- PrEP
- Cash Incentives
- Condoms
- Microbicides
- Vaccines
### HPTN Scientific Portfolio

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>HIV Status</strong></td>
<td>HIV negative, Acute Infection, Established HIV infection</td>
</tr>
<tr>
<td><strong>Populations</strong></td>
<td>Adolescents, MSM, women, pregnant women, IDU, communities</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Behavioral, HIV testing, PrEP, ART, VMMC, substitution/antagonist therapy, cash transfers</td>
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<tr>
<td><strong>Integrated Strategies</strong></td>
<td>US, Zambia &amp; South Africa</td>
</tr>
<tr>
<td><strong>Types of Studies</strong></td>
<td>Observational, individual randomized, site randomized, community randomized, implementation science</td>
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## HPTN Scientific Portfolio

<table>
<thead>
<tr>
<th>Biomedical</th>
<th>Behavioral</th>
<th>Structural</th>
<th>Integrated Strategies</th>
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<tbody>
<tr>
<td>HPTN 052</td>
<td>HPTN 061</td>
<td>HPTN 043</td>
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<td>HPTN 058</td>
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Foundational Research
HPTN 061: The BROTHERS Study
The first and largest prospective study of BMSM conducted in the U.S. Enrolled a total of 1,553 men in six U.S. cities. First study to clearly define HIV incidence rate for BMSM in the U.S.
Study Methods

- BMSM recruited from the community or referred by sexual partners
- Eligibility criteria:
  - Identified as a man, or were male at birth
  - Identified as Black, African American, Caribbean, African or multi-ethnic Black
  - At least 18 years old
  - At least one episode of unprotected anal intercourse with a man in the past six months
- Participants were offered incentives to refer up to 5 black sexual partners for participation in the study
Study Methods

- Demographic information collected and behavioral assessment using ACASI
- Social and sexual network questionnaire completed with an interviewer
- Tested for Gonorrhea, Chlamydia, Syphilis
- Risk-reduction counseling
- Offer of services of a peer community navigator to link to clinical and social services
- Participants testing positive for any infection linked to treatment and medical care services
Study Findings

- Non-adherence to HIV testing guidelines
  - reported by 23% of participants at enrollment; 14% reported never testing for HIV
  - associated with age > 35, unemployment, and not having seen a medical provider
- 97.5% of participants agreed to HIV testing
- 19% of participants with newly diagnosed HIV had a late HIV diagnosis (CD4 < 200)
- Late diagnosis was associated with age > 35
Study Findings

- HIV incidence among BMSM was 2.8% per year, 50% higher than rates in white MSM in the U.S.
- Young BMSM (< 30) acquired HIV infection at a rate of 5.9% per year, three times that of U.S. white MSM.
Conclusions

- Rates of undiagnosed HIV among BMSM were very high, representing a major health disparity.
- Structural, behavioral, and biological factors were independently associated with undiagnosed HIV infections.
- Culturally tailored programs for BMSM are urgently needed that encourage repeated HIV/STI testing, engagement in care, the use of ARV medications for treatment or prevention, while addressing social and environmental factors.
MY LIFE
MY HEALTH
MY CHOICE
HPTN 073 Study Design

- Demonstration project
- Planned enrollment
  - 225 participants
  - 75 participants per site
- All participants will be offered once daily oral Truvada® combined with client centered care coordination (C4)
Study Procedures

Engage and Educate

Test Negative

Support Adherence and Retain

Counsel, Link and Support
HPTN 073 CLINICAL RESEARCH SITE LOCATIONS
HPTN 073 Study Questions

• Will BMSM initiate PrEP?
  – Why or why not?

• Will BMSM use PrEP daily?
  – If not how often?

• Is it safe for BMSM to use PrEP?

• Will BMSM sexual practices change with uptake of PrEP?
Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?

How much Truvada® is in the blood of BMSM who become infected with HIV?

How often does HIV drug resistance occur?
Why Truvada®?

• Limited side effects
• Strong safety profile as therapy among HIV positive people
• Relatively long duration of action in the body (product “half-life”)
• Less likelihood of promoting drug resistance compared to other ARVs
Client Centered Care Coordination (C4)

- A clinical model maximizing resources and expertise of a healthcare team to develop a unique healthcare plan based on client needs.
- Considers experiences of BMSM in the U.S. related to biomedical interventions, psychosocial issues, and barriers to accessing health care.
Core Elements of C4

• **Care Coordination**: provides individualized prevention counseling, support, and service coordination working closely with service providers.

• **Client-Centered Approach to Care**: an approach in which each client’s realities are taken into consideration with the goal of optimizing retention and adherence.

• **Provider for Clinical Oversight**: different providers will perform different functions related to care coordination, the client-centered approach to care, and PrEP discussions/administration.
## Provider of Clinical Oversight

<table>
<thead>
<tr>
<th>Service</th>
<th>Provider(s)</th>
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<tbody>
<tr>
<td>Clinical assessment of PrEP suitability and PrEP health education</td>
<td>RN, PA or NP</td>
</tr>
<tr>
<td>Clinical monitoring and medical oversight</td>
<td>MD, RN, PA or NP</td>
</tr>
<tr>
<td>Substance abuse screening and appropriate referral</td>
<td>RN, PA, NP, SW or other trained staff</td>
</tr>
<tr>
<td>Coordinated linkage to psychosocial services and follow-up</td>
<td>RN, PA, NP, SW or other trained staff</td>
</tr>
<tr>
<td>Interim phone-based adherence support</td>
<td>RN, PA, NP, SW or other trained staff</td>
</tr>
</tbody>
</table>
BMSM in the Study

BMSM who meet all of the following criteria are eligible for inclusion in this study:
• 18 years of age or older
• Black, Caribbean Black, or a multi-ethnic Black male
• MSM
• HIV negative
• Male at birth and identify as male
• Sexually active
• Willing to provide comprehensive and current locator information
BMSM in the Study

- Participants will visit the clinic approximately 7 times during the study
- At each visit participants will
  - be offered the option of beginning/ending Truvada®
  - have a physical examination
  - discuss concerns or drug side effects
  - establish a care plan
  - receive HIV/STI counseling and testing
  - be offered condoms
BMSM in the Study

BMSM enrolled in this study should not:

• Participate in another biomedical HIV prevention study
• Share or sell Truvada® tablets
• Stop using condoms
Participant Visit Schedule

- Screening
- Enroll in C4 and offer PrEP
- 4 weeks
- 26 weeks
- 13 weeks
- 39 weeks
- 52 weeks
- 8 weeks
Length of Study

- The study will last 30 months from the time the first participant is enrolled until the researchers have results.
- Each participant will be followed for a total of 12 months.
Participant Interviews

- Individual semi-structured interview at each site
  - 5 participants who initiated PrEP
  - 5 participants who did not initiate PrEP
- Ascertain information about facilitators and barriers to the initiation, acceptability and adherence of PrEP
- Approximately 60 to 90 minutes
Staff Focus Groups

• Each site will conduct one focus group with the C4 team at the end of the study
• Will gather feedback on resources they believe are necessary to implement a C4-based PrEP program
  – Available onsite resources
  – Resources available in the community
  – Resources not available during the study
  – How resources would have improved provision of care
HPTN 073 Study Groups

Chapel Hill, NC
75 Participants
- 5 PrEP Uptake Interviews
- 5 PrEP Non-Initiator Interviews
- Site Staff C4 Focus Group

Los Angeles, CA
75 Participants
- 5 PrEP Uptake Interviews
- 5 PrEP Non-Initiator Interviews
- Site Staff C4 Focus Group

Washington, DC
75 Participants
- 5 PrEP Uptake Interviews
- 5 PrEP Non-Initiator Interviews
- Site Staff C4 Focus Group
Community Engagement

• Community engagement has been key at all stages of development and implementation:
  – Community input on protocol design
  – Community representatives on protocol team
  – HPTN 073 Community Working Group
  – Community consultations at each site
  – Community contacts/advocates
  – Ongoing community feedback
Antiretroviral (ARV) Drug Resistance
What is Resistance?

- ARVs stop HIV from making copies of itself
- Providers usually prescribe three ARV medicines simultaneously to stop HIV from making copies.
- Sometimes ARVs are not able to stop all of the HIV in a person’s body from making copies.
- Virus that is able to continue making copies of itself is called “resistant” to the ARV medicine that is being taken.
- This does not mean the virus is resistant to all types of ARV medicines.
Why is HIV Drug Resistance a Problem?

• When resistance happens, an ARV medicine is no longer able to stop HIV from making copies of itself.
• In this case, the person needs to stop taking the ARV medicine that is no longer working and start taking a different ARV medicine.
• A person who has resistant HIV has fewer choices of the ARV medicines that they can take to help them stay well.
Preventing HIV Resistance

• Use a condom every time you have sex
• Test for HIV regularly. HIV tests are provided at each HPTN 073 study visit.
• Do not share or sell your Truvada® tablets
HIV Testing Algorithm at Screening

- All Participants
- HIV Rapid Test
- Reactive
- Not Eligible
HIV Testing Algorithm at Screening

All Participants

HIV Rapid Test

Non-Reactive

HIV Diagnostic Test 2

Reactive

Not Eligible
HIV Testing Algorithm at Screening

- All Participants
  - HIV Rapid Test
    - Non-Reactive
      - Non-Reactive
        - Eligible
  - HIV Diagnostic Test 2
    - Non-Reactive

Eligible
HIV Testing Algorithm at Enrollment

All Participants

HIV Rapid Test

Reactive

Not Eligible
HIV Testing Algorithm at Enrollment

All Participants

HIV Rapid Test

Non-Reactive

Eligible
All Participants

HIV Rapid Test

Reactive

Possible HIV Infection

HIV Testing Algorithm at Follow Up Visits
HIV Testing Algorithm at Follow Up Visits

- All Participants
  - HIV Rapid Test
    - Non-Reactive
      - Confirmatory Test
      - Possible HIV Infection
    - Reactive
      - HIV Diagnostic Test 2
HIV Testing Algorithm at Follow Up Visits

All Participants

HIV Rapid Test

Non-Reactive

HIV Diagnostic Test 2

Non-Reactive

HIV Negative
Conclusions
Conclusions

• The HPTN has a strong commitment for quality research
• PrEP is one component of the Network’s diverse scientific portfolio
• Science will inform future community level studies and implementation of PrEP programs for BMSM
Clinical Research Site Information

- CRS Name
- Contact Person
- Address
- Phone Number
- Website
Additional Information

- www.hptn.org
  - www.facebook.com/HIVptn
  - www.twitter.com/HIVptn

- www.nih.gov

- www.cdc.gov
ACKNOWLEDGEMENTS

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MY LIFE
MY HEALTH
MY CHOICE