Update on the Science of ARV based HIV Prevention

JONATHAN PAUL LUCAS, MPH
SATURDAY, SEPTEMBER 7, 2013
NEW ORLEANS, LA
Overview

- Overview of HPTN
- PrEP
- HPTN PrEP Studies
  - HPTN 067
  - HPTN 069
  - HPTN 073
  - HPTN 076
- Treatment as Prevention (TasP)
  - HPTN 052
  - HPTN 065
- Conclusions
- Questions and Answers
HPTN Overview
HIV Combination Prevention

- 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
<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>
Pre- Exposure Prophylaxis (PrEP)
Background
PrEP (Pre-Exposure Prophylaxis) is a new approach that has shown 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 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
- ARVs for 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
CDC: Drug(s) for Prophylaxis

• Use the most effective drug(s).
• No drug is 100% protective; must combine with personal protective measures.
• Choose well-tolerated drug(s); minimize side effects.
• Consider concomitant conditions (e.g. pregnancy, renal disease).
• Consider the possibility of drug-drug interactions.
• Daily medicine often preferred.
• Least expensive.
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
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

Why Truvada®?
<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>
</tr>
<tr>
<td>Study (reference)</td>
<td>Study population</td>
<td>Design</td>
<td>Results</td>
</tr>
<tr>
<td>------------------</td>
<td>------------------------------------------</td>
<td>-------------------------------------------------</td>
<td>-----------------------------------------------------------------------</td>
</tr>
<tr>
<td>FEM-PrEP</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>MTN-003 (VOICE)</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>
HPTN Pre-Exposure Prophylaxis (PrEP) Studies
HPTN 067
The ADAPT Study: Alternative Dosing to Augment PrEP pill-Taking
Study Groups

1. Daily
2. Event-driven (before and after sex)
3. Time-driven (2 times a week and a booster after sex)

No more than
• 2 tablets in a 24-hour period
• 7 tablets in a week.
Daily
180 Participants
- 120 MSM
- 60 Women

Time Driven
180 Participants
- 120 MSM
- 60 Women

Event Driven
180 Participants
- 120 MSM
- 60 Women
Main Study Questions

• How does taking oral Truvada® tablets intermittently compare to taking the tablets daily? Will participants in the intermittent groups:
  – have the same coverage of sex events,
  – need fewer tablets for coverage, and
  – report fewer side effects compared to participants who take their tablets daily?
HPTN 069/ACTG 5305
NEXT-PREP:
Novel Exploration of Therapeutics for PREP

NEXT>PrEP
AN HPTN/ACTG STUDY
• There are 3 active drugs:
  – maraviroc (MVC)
  – emtricitabine (FTC)
  – tenofovir (TDF)

• Study Regimens (3 pills/arm):
  – maraviroc + FTC placebo + TDF placebo
  – maraviroc + emtricitabine + TDF placebo
  – maraviroc + tenofovir + FTC placebo
  – tenofovir + emtricitabine + MVC placebo
MVC
150
Participants
100 MSM
50 Women

MVC + FTC
150
Participants
100 MSM
50 Women

MVC + TDF
150
Participants
100 MSM
50 Women

FTC + TDF
150
Participants
100 MSM
50 Women
HPTN 069 Main Study Question

Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?
Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?

HPTN 069 Main Study Question
Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?

HPTN 069 Main Study Question

CUTE UNDERWEAR + CONDOM + PRE-EXPOSURE PROPHYLAXIS (PrEP)

HE INVITES YOU TO SPEND THE NIGHT. BE PrEPARED FOR WHAT HAPPENS NEXT.

FENWAY HEALTH
Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?

HPTN 069 Main Study Question

YOU’VE BEEN CHECKING HIM OUT ALL NIGHT. BE PrEPARED FOR WHAT HAPPENS NEXT.

FENWAY HEALTH
Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?

HPTN 069 Main Study Question

Antiretroviral therapies have transformed living with HIV.

Now, the same therapies may transform how we prevent it.

If you’re a man or trans-woman who has sex with men, join our expertly guided clinical trial for Pre-Exposure Prophylaxis (PrEP). Compensation provided.

3 pills. 1 year.
Real meds. Real hope.
The NEXT-PrEP Trial.

Learn more online at clevelandaids.org/prep.
Find us on Facebook at clevelandclinicaltrials. Or call 216.844.4444.
Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM) and at-risk women?

HPTN 069 Main Study Question

Antiretroviral therapies have transformed living with HIV.

Now, the same therapies may transform how we prevent it.

If you’re a man or trans-woman who has sex with men, join our expertly guided clinical trial for Pre-Exposure Prophylaxis (PrEP). Compensation provided.

3 pills. 1 year.
Real meds. Real hope.
The NEXT-PrEP Trial.

Learn more online at clevelandaids.org/prep.
Find us on Facebook at clevelandclinicaltrials.
Or call 216.844.4444.
HPTN 073: PrEP Adherence and Uptake Among BMSM in Three US Cities
HPTN 073 Study Design

- Demonstration project
- Once daily oral emtricitabine 200 mg / tenofovir disoproxil fumarate 300 mg (FTC/TDF)
- Client-centered care coordination (C4)
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
HPTN 073 Main Study Questions

- Will BMSM use PrEP?
- Is it safe for BMSM to use PrEP?
- Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?
HPTN 073 Main Study Questions

- Will BMSM use PrEP?
- Is it safe for BMSM to use PrEP?
- Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?
HPTN 073 Main Study Questions

• Will BMSM use PrEP?
• Is it safe for BMSM to use PrEP?
• Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?
HPTN 073 Main Study Questions

• Will BMSM use PrEP?
• Is it safe for BMSM to use PrEP?
• Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?
HPTN 073 Main Study Questions

- Will BMSM use PrEP?
- Is it safe for BMSM to use PrEP?
- Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?
HPTN 076: Injectable Pre-Exposure Prophylaxis (PrEP)
Study in Development

• Total of 132 participants at 4 sites
  – 48 at each international site
  – 18 at each US site
• Injectable PrEP vs placebo
HPTN 076 Main Study Questions

- Is injectable PrEP safe for women?
- Will women find injectable PrEP acceptable for use?
- Is injectable PrEP tolerable for women?
Treatment as Prevention (TasP)
PrEP builds on the concept that medications can be used by healthy people to prevent some infections—Malaria prophylaxis for travelers—Assumption that stopping HIV replication as soon as virus enters the body may prevent permanent infection

Why the Interest in PrEP?
HPTN 052: Serodiscordant Couples Study
HPTN 052 Study Design

Randomization

Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³

Immediate ART
CD4 350-550

Delayed ART
CD4 < 250

Primary Transmission Endpoint
Virally linked transmission events

Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death
Results of the HPTN052 trial announced on 12 May 2011 show that if an HIV-positive person adheres to an effective antiretroviral therapy regimen, the risk of transmitting the virus to their uninfected sexual partner can be reduced by 96%.

“Treatment for prevention is a game changer.”

Michel Sidibe
Executive Director of UNAIDS
Effective Implementation

Effective implementation of TasP requires addressing barriers to:

- Expanded testing,
- Improved care linkage and engagement
- Earlier ART initiation and adherence
HPTN 065: TLC Plus Test, Link to Care Plus Treat
HPTN 065: TLC-Plus Study

• A study to evaluate the feasibility of an enhanced test, link to care, plus treat approach for HIV prevention in the United States
  • Duration of study will not permit evaluation of changes in HIV acquisition rates
  • Study will use surveillance data, not individual participant-level data
HPTN 065 (TLC Plus) Study Design

HIV Testing & Linkage to Care
- Expanded 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
- Initiate ART per guidelines
  - 39 Randomized HIV Care Sites
  - Financial incentive plus SOC
  - Standard of care (SOC)

Prevention for Positives
- Select HIV Care Sites
  - Individual randomization of 1320 patients in 2 communities
  - CARE plus Standard of Care
  - Standard of Care
Expanded Testing

- Social mobilization to promote HIV testing
- Increase universal HIV screening of patients in
  - hospital emergency rooms
  - hospital inpatients.
- Increase the proportion of people tested for HIV
- Linked HIV infected to appropriate HIV care
- Supplements expanded testing efforts already underway
Expanded Testing

• Social mobilization to promote HIV testing
• Increase universal HIV screening of patients in hospital emergency rooms – hospital inpatients.
• Increase the proportion of people tested for HIV
• Link HIV infected to appropriate HIV care
• Supplements expanded testing efforts already underway
Linkage-to-Care (L2C)

- 37 HIV Test Sites were randomized for L2C
  - 18 in the Bronx, NY
  - 19 in Washington, DC

- Anyone newly found to be HIV-positive, or reconfirmed to be HIV-positive after having been out of care for at least one year, is eligible to receive a coupon at FI Test Sites

- $25 gift card for getting lab work done (CD4 and VL)

- $100 gift card for meeting with provider to review lab results and develop an individualized healthcare plan
Viral Suppression (VS)

- 39 HIV Care Sites were randomized for VS
  - 20 in the Bronx, NY
  - 19 in Washington, DC
- To receive VS gift cards, patients must be eligible for the program and then qualify for each gift card
- Patients are eligible if they are on ART and an established patient
- Patients qualify for a gift card if they have a suppressed viral load (<400 copies/mL) and have not earned a gift card in the last 3 months
Prevention for Positives

• Randomize HIV positive patients
  – computerized prevention intervention
  – standard-of-care prevention services
• Evaluate the effect of the prevention intervention on the frequency of risk behaviors
• Conducted at 12 sites (6 in each intervention community) with a total of 1,320 patients.
Patient Provider Surveys

- Survey HIV-positive patients receiving medical care
- Survey HIV care providers
- Assess their knowledge and attitudes regarding
  - the use of ARV medications for treatment and prevention of HIV
  - the use of financial incentives
- Survey 1,320 patients participating in the prevention for positives study component
- All providers at participating HIV care sites were invited to complete the provider survey
Conclusions
Conclusions

The HPTN has a strong commitment for quality research

• PrEP and TasP are components of the Network’s diverse scientific portfolio

• Science will inform future community level studies and implementation of PrEP and TasP programs
Additional Information

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

- www.nih.gov

- www.cdc.gov
Contact Information

Jonathan Paul Lucas, MPH
• 919-544-7040 ext 11458
• jlucas@FHI360.org
ACKNOWLEDGEMENTS

The HPTN is sponsored by NIAID, NIDA, NIMH under Cooperative Agreement #UM1 AI068619
ACKNOWLEDGEMENTS

The HPTN is sponsored by NIAID, NIDA, NIMH under Cooperative Agreement #UM1 AI068619.
ACKNOWLEDGEMENTS

The HPTN is sponsored by NIAID, NIDA, NIMH under Cooperative Agreement #UM1 AI068619