Combination Antiretroviral Prevention for MSM: A Biobehavioral Continuum

June 15, 2014
Crystal City, VA
Multifactorial Nature of MSM Risk

- **Biology**: Transmission probability
  - Per-act risk of anal sex is 18-fold greater than vaginal sex
  - Role versatility--receptive/insertive sex

- **Number of partners** over time

- **Networks**
  - Increased HIV/STI risk; Acute infection clusters
  - Assortative mixing--partners from similar racial/ethnic group
  - Sexualized venues--bathhouses, social media, sex work

- **Structural/Societal**
  - Homophobia, bullying, depression, risk perception
  - Criminalization and discrimination in care settings

## Drivers of HIV Transmission among MSM and Targets for Prevention

<table>
<thead>
<tr>
<th>Factor</th>
<th>Biomedical Interventions</th>
<th>Behavioral Interventions</th>
<th>Structural Enablers</th>
</tr>
</thead>
<tbody>
<tr>
<td>High biological risk of anal sex</td>
<td>Condoms, PEP, PrEP</td>
<td>↑condom use, PrEP adherence, ↓ EtOH and drug use</td>
<td>Condom distribution, CCHC, policy to support PrEP, drug treatment</td>
</tr>
<tr>
<td>High viral load in partners</td>
<td>ART for HIV+</td>
<td>↑ testing, linkage to care, access to ART, adherence counseling, retention in care</td>
<td>CCHC, stable supply chains, laboratory capacity for monitoring</td>
</tr>
<tr>
<td>High STI incidence</td>
<td>Screening and treatment</td>
<td>Uptake of screening</td>
<td>CCHC, provider training</td>
</tr>
<tr>
<td>Lack of awareness of HIV serostatus</td>
<td>HIV testing</td>
<td>Uptake of testing, disclosure of serostatus</td>
<td>CCHC, remove barriers to screening, structural disclosure approaches</td>
</tr>
<tr>
<td>High burden of behavioral health concerns</td>
<td>Medical rx. of depression, substance abuse</td>
<td>Evidence-based interventions to address behavioral health concerns</td>
<td>Stigma and harm reduction programs civic engagement, CCHC</td>
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</table>

Does HAART Decrease HIV Transmission for MSM?

- Overall HIV transmission rate
  - Zero through condomless sex with a partner on ART (HIV RNA <200 copies/mL), despite a significant number of sex acts

- Uncertainty over the upper limit of risk remains
  - Particularly with receptive anal sex with ejaculation

- Additional follow-up needed to provide more precise estimates for transmission risk
  - Duration of prior ART without transmission may have selected for lowest risk discordant couples

What do we need to know for an efficacy trial of TasP in MSM?

- How best to reach, test and link MSM, including young, minority, and hidden MSM
- How serious a challenge to TasP are patterns of mobility in MSM sexual partnerships
- For MSM living with HIV, what scalable interventions will most effectively increase linkage, retention, and rates of viral suppression
- What levels of ART coverage and viral suppression are needed to measurably reduce HIV incidence among MSM at community levels
# HPTN 078: HIV-Infected MSM Vanguard Study

<table>
<thead>
<tr>
<th>Study Components</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Surveillance</strong></td>
<td>Optimize recruitment: time venue-based vs. respondent-driven sampling</td>
</tr>
<tr>
<td></td>
<td>Availability and recent use of PEP and PrEP</td>
</tr>
<tr>
<td></td>
<td>Magnitude of migration outside city of residence</td>
</tr>
<tr>
<td><strong>Linkage and Retention</strong></td>
<td>Universal offer of ART</td>
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<tr>
<td></td>
<td>Evidence-based intensive case management, plus:</td>
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<tr>
<td></td>
<td>• Cognitive behavioral counseling</td>
</tr>
<tr>
<td></td>
<td>• 2-way text messaging</td>
</tr>
<tr>
<td></td>
<td>• Financial incentives, based on findings from HPTN 065</td>
</tr>
<tr>
<td><strong>Partner Notification</strong></td>
<td>Incentivize partner notification enabling cluster identification</td>
</tr>
<tr>
<td><strong>Modeling</strong></td>
<td>Interpret study results and project impact over extended time periods</td>
</tr>
</tbody>
</table>
Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention

(Calculations based on analyses involving a subset of total trial participants)

Pearson correlation = 0.86, p=0.003
Proportion of PrEP Users by State of Residence

Proportion of responders; darker shades of green indicate a higher proportion of participants. Not pictured: Alaska (0.2%) and Hawaii (0.6%)

N=9,179 1.2% had used PrEP

Circles indicate locations where PrEP use was reported and number of participants reporting PrEP use in that location.
# Phase 3/4 PrEP Research and Demonstration Projects in MSM

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Duration</th>
<th>Location</th>
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<tbody>
<tr>
<td><strong>Ongoing Phase 3 Studies</strong></td>
<td></td>
<td></td>
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<tr>
<td>IPERGAY</td>
<td>1900</td>
<td>24 months</td>
<td>France, Canada</td>
</tr>
<tr>
<td><strong>Demonstration Projects and Open-Label Extensions (planned and ongoing)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAIDS PrEP MSM Demo</td>
<td>557</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>CDC PrEP Demo</td>
<td>600</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>PROUD</td>
<td>5000 (500 as pilot)</td>
<td>12 months on tx, 12 month follow-up</td>
<td>U.K.</td>
</tr>
<tr>
<td>Project PrEPare 110</td>
<td>200</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>SFDPH EPIC PrEP</td>
<td>300</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>ALERT</td>
<td>400</td>
<td>12 months+</td>
<td>U.S.</td>
</tr>
<tr>
<td>Los Angeles PATH</td>
<td>300</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>Hunter College PrEP</td>
<td>250</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>NYC PrEP</td>
<td>200</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>Brazilian PrEP</td>
<td>500</td>
<td>12 months</td>
<td>Brazil</td>
</tr>
<tr>
<td>Rio PrEP</td>
<td>65</td>
<td>12 months</td>
<td>Brazil</td>
</tr>
<tr>
<td>HPTN 073</td>
<td>225</td>
<td>12 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>HPTN 069**</td>
<td>400</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>HPTN 067**</td>
<td>567</td>
<td>34 weeks</td>
<td>U.S., Thailand, S. Africa</td>
</tr>
</tbody>
</table>

*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)
**Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)
# Phase 3/4 Research and Demonstration Projects in MSM - Continued

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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HVTN 505</td>
<td>1000</td>
<td>5 years</td>
<td>U.S.</td>
</tr>
<tr>
<td>Fenway PrEP Adherence</td>
<td>50</td>
<td>6 months</td>
<td>U.S.</td>
</tr>
<tr>
<td>CRUSH</td>
<td>170</td>
<td>48 weeks</td>
<td>U.S.</td>
</tr>
<tr>
<td>PrEP in STD Clinics***</td>
<td>50</td>
<td>18 months</td>
<td>U.S.</td>
</tr>
</tbody>
</table>

**TOTAL: 19**

12,734

*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)*

**Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)**

***Includes MSM; serodiscordant couples and sex workers (men and women)***
Strategies to improve PrEP delivery and adherence

New PrEP drugs and dosing strategies

Vaginal & Rectal Microbicides: MTN-017 (TFV rectal gel)

Intra-vaginal rings: ASPIRE (Dapivirine)

Injectables: Rilpivirine-LA Cabotegravir HPTN 076, 077

Alternative delivery systems and formulations

Novel adherence strategies

NEXT PrEP

ADAPT

The Future

- STD clinics in San Francisco, Miami, Washington, DC (n=831)
  - MSM, transgender women (1.4%)
  - Clinic referrals (63%)
  - Self-referrals (37%): more likely to be white, higher education level, higher sexual risk behaviors and risk perception versus clinic referrals

- Offered up to 48 weeks of open-label emtricitabine/tenofovir DF
  - Accepted PrEP: 60.4%
    - 77% had TDF-DP levels consistent with taking ≥4 doses/week

- PrEP uptake associated with
  - Self-referral, prior PrEP awareness, higher-risk sexual behaviors

BLD: below limit of detection.


* femtomole/punch: measure of flux density.
Southern California: Path-PrEP: Staged Adherence (R Landovitz)

All participants will receive "Opt-in" adherence challenges discussion

Adherence assessed by:

4-day participant recall/pill count

Real-time serum levels of TFV/FTC

If serum TFV < 10 ng/mL, Next-Step Counseling Intervention (NSC)

Repeat TFV levels <10 ng/mL, "PrEP-STEP" program

DBS for intra-erythocytic TFV levels
Project PrEPare (NIMH R34, Fenway)

- Modeled after “Life-Steps,” (Safren et al) ART adherence intervention
- Modular intervention: 4 weekly visits and 2 booster sessions (nurse-delivered).
- Intervention content:
  - CBT-oriented adherence problem-solving
  - Brief motivational interviewing
  - Identification of barriers and solutions
  - Sexual risk-reduction strategies
- Optional modules:
  - Mental health and substance use concerns

- Adherence to PrEP was measured daily via Wisepill
- Sexual risk taking was assessed by text messages (Lester, 2010)
Beyond HPTN 061: Tailoring PrEP for Black MSM

Annual HIV incidence 3%; for 18-29 y.o. 5.9%

High rates of STIs, associated with HIV

Many men with advanced HIV were identified
- Mannheimer S et al, AIDS 2012, MS under review

Many unmet social needs, poverty, incarceration
We’ve launched a new PrEP demonstration project for Black men who have sex with men.

Participate in the live Twitter chat on

Wednesday, August 14
at 10 am PT / 1 pm ET

With our guests: @JonPaulLucas and @cchauncey

Be sure to follow @HIVptn

Join the HPTN 073 Webinar:

“Introducing HPTN 073: A BMSM PrEP Demonstration Study”
at 11 am PT / 2 pm ET
by registering at


Find out more about HPTN 073 at
www.HPTN.org and at Facebook/HIVptn
HPTN 080: Purpose and Teams

- **Purpose:**
  - To assess the impact of one combination prevention package on PrEP uptake, and a second package on adherence and persistence to PrEP, among HIV-uninfected MSM and transgender women in North and South America.
  - To assess the acceptability/desirability of individual components of the packages, as well as interactions between the two packages.

- **Core Writing Team:** S Buchbinder, S Eshleman, L Greene, J Hughes, A Liu, E Piwowar-Manning, H Scott, S Wolf, E Vittinghoff

- **Additional PT members:** L Emel, S Fields, B Grinzjstein, R Irvin, J Lucas, L McKinstry, G Millett, J Sanchez, P Sullivan, V Veloso, D Wheeler
HPTN 080: Study Design

HIV-uninfected MSM and TGW, North and South America

SexPro PrEP Uptake Intervention

PrEP Plus Adherence Support Intervention
- Standard of Care

PrEP Plus Adherence Support Intervention
- Standard of Care

Control
Part 1: Uptake interventions

1. **SexPro**: Online risk assessment and sexual health promotion score.

2. **BlackBook**: Sexual diary mobile phone app.

3. **Online tools**: Video interviews of MSM, TGW who have opted to take or not take PrEP, PrEP information
Part 2: Adherence Interventions

1. **SMS**: Regular check in ("Are you okay") to triage participants needing support, based on Lester WelTel system used in Kenya that improved treatment adherence.

2. **PrEP Forum**: Asked for by many participants to share information, strategies.

3. **Online Tools**: PrEP Starter Pak, videos, online tools.

- 3 month pilot study in iPrEx OLE (SF and Chicago)
- 50% reduction in missed doses comparing periods before/after intervention (self-report and pill count)
Mental Health / Substance Use Can Interfere with Health Behavior Intervention Models

Depression / Anxiety, poverty, poor social conditions, substance use dx

Information
Behavioral Skills
Health behavior / Adherence
Motivation

Combination Antiretroviral Prevention

Interventions to Increase Testing

Test

HIV Negative

Risk Assessment
PrEP, Adherence
Counseling

Address concomitant concerns:
depression, substance use, relationship
dynamics

HIV Positive

Positive Prevention

Linkage To Care

Enroll in Care

ART Initiation

Treat

Adherence to ART

Maintain Viral Suppression

Decrease in HIV Transmission
Thank You

Salim Abdool Karim
Rachel Baggaley
Chris Beyrer
Susan Buchbinder
Deborah Donnell
Wafaa El-Sadr
David Glidden
Robert Grant
Doug Krakower
Raphy Landovitz
Albert Liu
David Novak
Steve Safren
Patrick Sullivan

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