CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS

HIV

Avoiding the Cost of Inaction

18-19 September 2014 • Royal Garden Hotel, London
Antiretroviral Chemoprophylaxis: State of the Evidence

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Beth Israel Deaconess Medical Center
Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention

Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Source: Salim S. Abdool Karim, CAPRISA
PrEP clinical questions

Symptoms: Start-up, GI, uncommon

Renal: uncommon with monitoring

Bone: focus on youth ATN 110/113

Selection for resistance: rare, almost all 184V

Risk compensation vs. reaching those at risk

Other STI: need for frequent monitoring; HSV-2?

Other approaches: Two ring studies; FACTS 001
Ongoing and Planned Phase 3/4 Research, Including Demonstration Projects

- Phase 3 studies are continuing to evaluate PrEP in various demographic groups
- Gilead is committed to post-marketing demonstration studies in the U.S. and globally
- Collaborators: ANRS, CDC, FHI, MRC, NIAID (DAIDS), NICHD (ATN), SFDPH, U. Washington, and Gilead Sciences

<table>
<thead>
<tr>
<th>Population</th>
<th>Studies</th>
<th>Participants</th>
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<tbody>
<tr>
<td>MSM</td>
<td>17</td>
<td>14,100</td>
</tr>
<tr>
<td>Heterosexual Men &amp; Women</td>
<td>8</td>
<td>10,201</td>
</tr>
<tr>
<td>Serodiscordant Couples</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>25</td>
<td>24,301</td>
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ANRS = French National Agency for AIDS Research; CDC = Centers for Disease Control and Prevention; FHI = Family Health International; MRC = Medical Research Council (UK); NIAID = National Institute of Allergy and Infectious Diseases; DAIDS = Division of AIDS; NICHD = National Institute of Child Health and Human Development; SFDPH = San Francisco Department of Public Health
High Levels of Adherence are Feasible: US PrEP Demonstration Project: (2012-2014)

- 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.

iPrEx Open-Label Extension (OLE): HIV Incidence and Predictors of Detectable Drug

- HIV incidence in iPrEx OLE
  - PrEP versus no PrEP
    - 1.8 versus 2.6 infections/100 person-years (adjusted HR: 0.51, 95% CI: 0.26-1.01)
  - PrEP, but no drug detected
    - 4.7 infections/100 person-years
- HIV incidence in original iPrEx: placebo recipients
  - 3.9 infections/100 person-years

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<tr>
<th>Predictors of Detectable Drug</th>
<th>Adjusted Odds Ratio</th>
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<tr>
<td>Non-condom intercourse (reference: none)</td>
<td></td>
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<tr>
<td>Receptive, anal</td>
<td>1.66 (P&lt;0.0001)</td>
</tr>
<tr>
<td>Male sexual partners (reference: 0-1)</td>
<td></td>
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<tr>
<td>2-4</td>
<td>1.33 (P=0.005)</td>
</tr>
<tr>
<td>≥5</td>
<td>1.82 (P&lt;0.0001)</td>
</tr>
<tr>
<td>Age (reference: 18-24 years)</td>
<td></td>
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<tr>
<td>30-39</td>
<td>1.64 (P=0.0002)</td>
</tr>
<tr>
<td>≥40</td>
<td>3.29 (P&lt;0.0001)</td>
</tr>
<tr>
<td>Education (reference: &lt;secondary)</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>1.99 (P&lt;0.0001)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>1.93 (P&lt;0.0001)</td>
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</table>

Grant RM, et al. 20th IAC. Melbourne, 2014. Abstract TUAC0105LB.

Lively Discussion and Debate in the Blogosphere

Project Inform launches new educational video series on PrEP!

Making decisions to take PrEP with your doctor.  
Figuring out how PrEP fits into your life.

• Brief video testimonials developed regarding PrEP users’ decisions and motivations to take PrEP and experiences taking PrEP

• Also: [www.myprepexperience.blogspot.com](http://www.myprepexperience.blogspot.com)  AIDS Foundation of Chicago
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.
## Factors Associated with PrEP Use among US MSM

Multivariable Model, Manhunt Survey, CROI, 2014

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<tr>
<th>Characteristic</th>
<th>Multivariable OR (95% CI)</th>
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<tr>
<td>College graduate or above (vs. less than college education)</td>
<td>5.33 (1.25 to 22.7)</td>
</tr>
<tr>
<td>Ever diagnosed with an STI</td>
<td>2.74 (1.36 to 5.52)</td>
</tr>
<tr>
<td>Used PEP</td>
<td>16.0 (8.24 to 31.2)</td>
</tr>
<tr>
<td>Comfortable talking with provider about MSM sex</td>
<td>4.19 (1.51 to 11.6)</td>
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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)
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
- DBS for intra-erythocytic TFV levels

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

Repeat TFV levels <10 ng/mL, “PrEP-STEP” program
U.S. Black MSM and PrEP: Lessons from  HPTN 061

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
**PrEP Uptake Among Young MSM**

- Chicago cohort of young, primarily Black MSM

- 2/3 of those in earlier ATN trial enrolled in iPeEX Ole with choice of PrEP use or not

- 70% of those YMSM elected to take PrEP

- Drug detection ↑ from 45% to 58% and 70% expressed interest in ongoing PrEP use

Hosek, CROI, 2014
Purview paradox: contradictory beliefs about which providers will prescribe PrEP
(Krakower, AIDS and Behavior, 2014)

HIV providers:
Primary care providers are in the best position to prescribe PrEP

Primary care providers:
It would not be feasible to prescribe PrEP
New England providers perceived numerous barriers to prescribing PrEP (Krakower, Adherence 2014)

- Lack of patient requests: 7% not a barrier, 22% minor barrier, 45% moderate barrier, 26% major barrier.
- Concerns about insurance coverage: 10% not a barrier, 26% minor barrier, 31% moderate barrier, 32% major barrier.
- Clinicians not trained to prescribe PrEP: 14% not a barrier, 22% minor barrier, 30% moderate barrier, 35% major barrier.
- Clinicians not aware of CDC guidance: 19% not a barrier, 22% minor barrier, 33% moderate barrier, 25% major barrier.
- Time constraints: 22% not a barrier, 38% minor barrier, 31% moderate barrier, 9% major barrier.
- Clinicians not aware of PrEP: 23% not a barrier, 27% minor barrier, 31% moderate barrier, 20% major barrier.
- Limited # at-risk patients: 27% not a barrier, 33% minor barrier, 25% moderate barrier, 15% major barrier.

Numbers represent percentage for each response category: not a barrier, minor barrier, moderate barrier, major barrier. Bars total to 100%.
New Technologies may provide tools for more efficient risk screening

**HIRI-MSM Risk Index**

1. How old are you today (yrs)?
   - < 18 years: score 0
   - 18-28 years: score 8
   - 29-40 years: score 5
   - 41-48 years: score 2
   - ≥49 years: score 0

2. How many men have you had sex with in the last 6 months?
   - > 10 male partners: score 7
   - 6-10 male partners: score 4
   - 0-5 male partners: score 0

3. In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?
   - 1 or more times: score 10
   - 0 times: score 0

4. How many of your male sex partners were HIV positive?
   - > 1 positive partner: score 8
   - 1 positive partner: score 4
   - < 1 positive partner: score 0

5. In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?
   - 5 or more times: score 6
   - 0 times: score 0

6. In the last 6 months, have you used methamphetamine such as crystal or speed?
   - Yes: score 5
   - No: score 0

7. In the last 6 months, have you used poppers (amyl nitrate)?
   - Yes: score 3
   - No: score 0

Add down entries in right column to calculate total score

**Electronic Patient Reported Outcomes, CNICS**

H. Crane

D. Smith JAIDS 2012
Cost of PrEP is going down globally

17 generic partners are licensed to manufacture and sell Gilead therapies; market competition has helped reduce the cost of TDF by 80% since 2006
The PrEP cascade (A Liu et al)

1. At risk for HIV infection
2. Identified as PrEP candidate
3. Interested in PrEP
4. Linked to PrEP program
5. Initiated PrEP
6. Retained in PrEP Program
7. Achieve adherence and persistence
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
    - Linkage To Care
    - Positive Prevention

- Enroll in Care
  - ART Initiation
  - Treat
    - Adherence to ART
  - Maintain Viral Suppression

Decrease in HIV Transmission
PrEP in 2014

- PrEP works when used consistently
- No new safety signals; Bone health under study
- Demo projects underway in many parts of the world
- Early demonstration projects suggest that those who present for PrEP may be motivated to adhere
- Optimizing social media may facilitate safer sex and med adherence counseling
- Providers need more education about PrEP
- Use of generics and focusing on highest risk will ↓cost
- New PrEP meds/modalities may ↑uptake, ↓cost
Many thanks

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www.thefenwayinstitute.org