9th International Conference on HIV Treatment and Prevention Adherence

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IAPAC
INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

PIM
Postgraduate Institute for Medicine
PrEP: State of the ART

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Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention

Effectiveness (%)

Percentage of participants' samples that had detectable drug levels

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

Pearson correlation = 0.86, p=0.003
Residual PrEP Concerns

- **Risk Compensation**: not seen in trials
- **Renal insufficiency**: rare, reversible
  - but pts had to have normal function for trials
- **Bone demineralization**: statistically significant, not clinically significant at 18 months, needs f/u
- **Transmission of resistance**
  - Primarily in pts started on PrEP with acute HIV
  - Most were 184V (3TC/FTC $^R$, less fit virus)

Role of Genital Tract Inflammation and PK need f/u

(Naranbhai, JID, 2012; Hendrix, CROI, 2014)
Assessment of Truvada for PrEP Utilization in the US

- Geographically prescribers of TVD for PrEP are located in 49 states and distributed across approximately 700 cities.
- Only 37% also prescribed Truvada for HIV treatment.
- Overall, 6 specialties initiated 75.6% of PrEP prescriptions:
  - Family Practice 16%
  - Internal Medicine 15%
  - Emergency Medicine 14%
  - Infectious Diseases 12%
  - Nurse Practitioners 9%
  - Physician Assistants 8%
- When compared to HIV positive patients, uninfected individuals receiving TVD for PrEP were:
  - 1.4 times more likely to be from the South (95% CI 1.3 – 1.6)\(^a\)
  - 1.8 times more likely to be female (95% CI 1.7 – 2.0)\(^b\)
  - 1.4 times more likely to be younger than 25 years old (95% CI 1.2 – 1.6)\(^b\)
  - 3.8 times more likely to be treated by a non-ID physician (95% CI 3.3 – 4.2)\(^a\)

\(^a\) multivariate logistic model  \(^b\) p < 0.01

Mera et al. ICAAC 2013. Denver, CO. Poster H663a
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>
</tr>
</thead>
<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>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25</strong></td>
<td><strong>24,301</strong></td>
</tr>
</tbody>
</table>

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

- 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.


Tenofovir-DP Levels (Week 4)
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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Multivariable OR (95% CI)</th>
</tr>
</thead>
<tbody>
<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>
</tr>
</tbody>
</table>
PrEP Culture Wars?

"IF A PERSON TAKES TRUVADA [AS PrEP] WHEN THEY ARE SUPPOSED TO, AND THEY TAKE IT EVERY DAY, THEN THEIR CHANCE OF BECOMING INFECTED WITH HIV IS CLOSE TO ZERO."

- MICHAEL WEINSTEIN
NOVEMBER 9, 2013

LEARN THE FACTS FROM A RELIABLE SOURCE. MORE INFO AT PREPFACTS.ORG

THE STIGMA PROJECT
Reality: Lively Discussion in the E-Universe

Project Inform launches new educational video series on PrEP!

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

• Also: www.myprepexperience.blogspot.com  AIDS Foundation of Chicago

• https://www.facebook.com/groups/PrEPFacts
INTRODUCING THE “PrEP PACKAGE” FOR ENHANCED HIV PREVENTION:
A Practical Guide for Clinicians
October, 2012

THE FENWAY INSTITUTE

PROTECTING YOURSELF FROM HIV THROUGH PRE-EXPOSURE PROPHYLAXIS (PrEP):
What You Need to Know
October, 2012

THE FENWAY INSTITUTE

- www.thefenwayinstitute.org

WHAT IS PrEP?
PrEP is recommended as one prevention option for sexually-active adult MSM (men who have sex with men) at substantial risk of HIV acquisition \(^{(IA)}\)

PrEP is recommended as one prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition. \((IA)\)

PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition. \((IA)\)

PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus \((IIB)\)
Strategies to improve PrEP delivery and adherence

New PrEP drugs and dosing strategies

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

Injectables: Rilpivirine-LA GSK744

Alternative delivery systems and formulations

Novel adherence strategies

Intra-vaginal rings: ASPIRE (Dapivirine)

The Future
NEXT EXIT

NEXT PrEP
AN HPTN067G STUDY

ADAPT
HPTN067
<table>
<thead>
<tr>
<th>Issue</th>
<th>The Pill (Envoid)</th>
<th>TDF/FTC (PrEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st year on market</td>
<td>1957 (infertility)</td>
<td>2004 (treatment)</td>
</tr>
<tr>
<td>Year of FDA approval for prevention</td>
<td>1960</td>
<td>2012</td>
</tr>
<tr>
<td>N pts included in FDA filing</td>
<td>897 women</td>
<td>76919 men &amp; women</td>
</tr>
<tr>
<td>Median time on med for pts included in FDA filing</td>
<td>&lt;1 yr</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Monthly cost</td>
<td>$77</td>
<td>$1425 in US $6 in LMIC</td>
</tr>
</tbody>
</table>

Sepkowitz and Myers, CID, 2013
TFV-DP Concentrations in IPrEx and STRAND

Regression analysis in iPrEx: 90% reduction in HIV acquisition when TFV-DP > 16 fmol/10^6 cells

Predicted risk reduction:
- 76% with 2 pills/week
- 96% with 4 pills/week
- 99% with 7 pills/week

* Visit when HIV was first discovered

Anderson et al, Science Translational Medicine 2012 4:151ra125
Less than daily TDF/FTC for PrEP?

- HPTN 066: assessed dose proportionality: takes time to accumulate and lose intracellular drug
- HPTN 067: MSM in NYC and Bangkok, women in Cape Town: assessing fixed interval vs. pericoital PrEP acceptability, not efficacy
- iPREGAY: Placebo controlled trial of pericoital TDF/FTC in French, German, Quebecois MSM
- No efficacy data yet, but drug level determinations in demonstration projects will be informative, full scale RCT will require resources
- Data suggest “forgiveness” but threshold not established
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

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 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

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

Southern California: Path-PrEP: Staged Adherence (R Landovitz; see Kofron, Session 12)
PrEP and Black MSM (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
To implement PrEP successfully, it will be essential to engage practicing clinicians.
Purview paradox: contradictory beliefs about which providers will prescribe PrEP
(see Krakower and Flash in Session 16 today)

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 barrier, 22% minor barrier, 45% moderate barrier, 26% major barrier.
- Concerns about insurance coverage: 10% not barrier, 26% minor barrier, 31% moderate barrier, 32% major barrier.
- Clinicians not trained to prescribe PrEP: 14% not barrier, 22% minor barrier, 30% moderate barrier, 35% major barrier.
- Clinicians not aware of CDC guidance: 19% not barrier, 22% minor barrier, 33% moderate barrier, 25% major barrier.
- Time constraints: 22% not barrier, 38% minor barrier, 31% moderate barrier, 9% major barrier.
- Clinicians not aware of PrEP: 23% not barrier, 27% minor barrier, 31% moderate barrier, 20% major barrier.
- Limited # at-risk patients: 27% not 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%.
A tool for risk-stratifying MSM: CDC risk index ("HIRI-MSM")

<table>
<thead>
<tr>
<th>HIRI-MSM Risk Index*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 How old are you today (yrs)?</td>
</tr>
<tr>
<td>&lt;18 years</td>
</tr>
<tr>
<td>18-28 years</td>
</tr>
<tr>
<td>29-40 years</td>
</tr>
<tr>
<td>41-48 years</td>
</tr>
<tr>
<td>≥49 years</td>
</tr>
<tr>
<td>2 How many men have you had sex with in the last 6 months?</td>
</tr>
<tr>
<td>&gt;10 male partners</td>
</tr>
<tr>
<td>6-10 male partners</td>
</tr>
<tr>
<td>0-5 male partners</td>
</tr>
<tr>
<td>1 or more times</td>
</tr>
<tr>
<td>0 times</td>
</tr>
<tr>
<td>3 In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?</td>
</tr>
<tr>
<td>&gt;1 positive partner</td>
</tr>
<tr>
<td>1 positive partner</td>
</tr>
<tr>
<td>&lt;1 positive partner</td>
</tr>
<tr>
<td>5 or more times</td>
</tr>
<tr>
<td>0 times</td>
</tr>
<tr>
<td>4 How many of your male sex partners were HIV positive?</td>
</tr>
<tr>
<td>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?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>6 In the last 6 months, have you used methamphetamines such as crystal or speed?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>7 In the last 6 months, have you used poppers (amyl nitrate)?</td>
</tr>
<tr>
<td>Add down entries in right column to calculate total score</td>
</tr>
</tbody>
</table>

Score < 9: standard prevention
Score ≥ 10: consider PrEP

Smith JAIDS 2012
Diffusion of Innovations

(Everett Rogers, 1962)
Innovation, Communication Channels, Time, Social System
We may not know what adherence will look like for the typical PrEP user for several years.
Non-Trial PrEP Uptake at Fenway Health

The graph shows the non-trial PrEP uptake at Fenway Health from 2011 to 2014. The number of patients taking PrEP increased significantly from 2011 to 2014, with a peak in 2013.
### Sociodemographics of Fenway Health PrEP Patients

- **MSM except for 2 transgender women**

- **Only Whites initiated in 2011 by 2013, 24.4% non-White, with ~8% each among Black, Latino, multiracial MSM**

- **3% <20 y.o.; 38% 20-29 y.o.; 28% 30-40 y.o.**

- **90% commercially insured; 4% Medicaid; 2% self-pay**
Combination Antiretroviral Prevention

Interventions to Increase Testing

Test

HIV Negative
Risk Assessment
PrEP, Adherence Counseling

HIV Positive
Positive Prevention

Linkage To Care

Enroll in Care
ART Initiation

Treat
Adherence to ART

Maintain Viral Suppression

Decrease in HIV Transmission

Address concomitant concerns:
depression, substance use, relationship dynamics
Thank You

Fenway Clinical, Epidemiological and Behavioral Research Teams
Fenway Medical Department

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Rivet Amico
Susan Buchbinder
Charlene Flash
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Chris Grasso
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Albert Liu
Beryl Koblin
Matthew Mimiaga
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Jim Rooney
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Dawn Smith
Darrell Wheeler

NIAID, NIMH, NIDA, NICHD, CDC, HRSA, Mass DPH, Gilead
www.thefenwayinstitute.org