Decreasing Population-Level HIV Incidence: The Role of Multifaceted HIV Prevention

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Fenway Health/Harvard Medical School

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Disclosures

- Unrestricted research grants from Gilead Sciences and ViiV Health Care

- Scientific Advisory Boards focused on HIV Prevention: Gilead Sciences and Merck Pharmaceuticals
Where are we in mid-2018?

• Proof of concept for TasP and PrEP in RCTs
• Demo Projects have shown promise
• Population-level impact seen in some jurisdictions
• Roll-out has highlighted disparities
• Roll-out has highlighted needs address behavioral and comprehensive sexual health to achieve global impact
The Key Paradigm: Test and Treat (when ready)

HPTN 052: Treatment as Prevention → Public Health Benefit → Begin treatment at any CD4+ T-cell count

START and Temprano Studies: Early Treatment → Individual Health Benefit
Why PrEP? In the TasP Era, Reductions in New HIV Infections are Off Target

*The 2020 target is fewer than 500,000 new HIV infections, equivalent to a 75% reduction since 2010.
Source: UNAIDS 2017 estimates.
GLOBAL HIV TRENDS

- 1995: 3 million new infections/year
  18 million PLHIV; 2 million deaths/year

- 2018:< 2 million new infections/year;
  39 million PLHIV; < 1 million deaths/year

- About half on HAART, but viral suppression variable

- 2.3 % ↓ in new infections 2005-2015

- 47% ↓ in death 2005-2015

- Since 2012, global HIV spending ↓ by 5.4%
Select Daily Oral TDF/FTC PrEP Trials: Effectiveness Improves With Adherence

*Reduction in HIV incidence vs control.
†Based on pill counts or the detection of study drug in plasma.

Fonner VA, et al. AIDS. 2016
PROUD Study: High PrEP Efficacy in a Real-World Setting

• Significantly ↓ HIV infections with immediate vs deferred PrEP (3 versus 20 cases)
  – HIV infection predated PrEP start (n=1)
  – No drug/not adherent (n=2)
• Number needed to treat to prevent 1 HIV infection: 13
• PrEP was generally well tolerated

Oral PrEP global roll-out, 2018

- National roll-out: Australia, Belgium, Brazil, Canada, Kenya, New Zealand, Norway, Scotland NHS, South Africa (US)
- Other implementation (e.g. demonstration projects, pharmacy access, DREAMS)
Number of people taking PrEP globally

Cumulative number starting PrEP

Estimated active users Feb 2018

Half of PrEP users are in the U.S.
HIV Decline at Dean Street - UK

80% decline in HIV cases since 2015
EPIC-NSW Cohort (N=3700): Targeted PrEP Decreasing HIV Incidence

- Medication possession ratio over 12 months (having enough medication to take PrEP over 12 months)
  - Mean: 83% (95% CI 82%-84%)

- Within cohort HIV infection rate: 0.5/100 person-years
  - 2 infections over 3927 person-years
    - 1 never commenced PrEP
    - 1 took no PrEP for months prior to infection

- Population change in HIV diagnoses over the past 12 months: 32% decline (from 149 to 102 persons)
  - Least reductions
    - Young MSM
    - MSM living outside the central Sydney “gay” suburbs
    - Non-English speaking overseas-born gay men

### Reduction in HIV Diagnoses (12-month before-after recruitment)

<table>
<thead>
<tr>
<th></th>
<th>Decline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>32</td>
</tr>
<tr>
<td>Years of age</td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>10</td>
</tr>
<tr>
<td>25-34</td>
<td>22</td>
</tr>
<tr>
<td>35-44</td>
<td>44</td>
</tr>
<tr>
<td>&gt;44</td>
<td>48</td>
</tr>
<tr>
<td>Country/region of birth</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>49</td>
</tr>
<tr>
<td>High-income, English speaking</td>
<td>33</td>
</tr>
<tr>
<td>Asia</td>
<td>21</td>
</tr>
<tr>
<td>Other countries</td>
<td>+24</td>
</tr>
<tr>
<td>Area of residence</td>
<td></td>
</tr>
<tr>
<td>Gay Sydney suburbs</td>
<td>52</td>
</tr>
<tr>
<td>Other Sydney</td>
<td>7</td>
</tr>
<tr>
<td>Outside of Sydney</td>
<td>54</td>
</tr>
</tbody>
</table>

~164,000 patients are taking Truvada for PrEP®

Individuals Taking Truvada for PrEP (Active) (000’s)

Individuals Initiating Truvada for PrEP

10.8k

- City-wide getting to zero consortium
  - Coordinated PrEP program
  - Rapid ART program
  - Linkage-engagement in care
- New HIV diagnoses in SF decreased 51% between 2012 (n=453) to 2016 (n=223)
  - Decreases seen among all race/ethnicity groups

PrEP candidates: HIV negative and condomless anal sex OR STI OR HIV-positive partner.
Adherence in clinical practice

- Refill-based PrEP adherence at Kaiser: **92%**! with >900 pts f/u
- <5% with <60% adherence (<4/week)
- 2 seroconversions b/c insurance lapses; none among those still on PrEP

### Factors associated with <80% adherence (N=915)

<table>
<thead>
<tr>
<th></th>
<th>Risk ratio*</th>
<th>(95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic Black</td>
<td>3.0</td>
<td>(1.7-5.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PrEP copay &gt;$50 per month</td>
<td>2.0</td>
<td>(1.2-3.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.6</td>
<td>(1.1-2.3)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

* Risk ratios obtained from Poisson regression with robust variance and adjusted for age, sex, race/ethnicity, socioeconomic status, copay, smoking, drug/alcohol abuse, baseline STI, baseline renal function, hypertension, and diabetes
HIV Acquisition after PrEP Discontinuation (Montreal)

- Retrospective cohort study in MSM who initiated PrEP and returned for at least 1 follow-up visit

**FIGURE 1**

- Individuals initiating PrEP
  - (N=1258)
  - Consistent PrEP use: 36% (N=450)
  - Periodic PrEP use: 9% (N=114)
  - Reported PrEP stop: 17% (N=214)
  - Lost to follow-up: 38% (N=480)
Persistency has dramatically improved over time – roughly half of patients still on Truvada for PrEP® after 1 year.

Average number of Truvada for PrEP refills/year = 7.5
Blacks Have Highest Number Needing PrEP in US

**ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015**

<table>
<thead>
<tr>
<th></th>
<th>Gay, bisexual, or other men who have sex with men</th>
<th>Heterosexually active adults</th>
<th>Persons who inject drugs</th>
<th>Total by race/ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black/African American, non-Hispanic</td>
<td>309,190</td>
<td>164,660</td>
<td>26,490</td>
<td>500,340</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>220,760</td>
<td>46,580</td>
<td>14,920</td>
<td>282,260</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>238,670</td>
<td>36,540</td>
<td>28,020</td>
<td>303,230</td>
</tr>
<tr>
<td>Total who could potentially benefit from PrEP</td>
<td>813,970</td>
<td>258,080</td>
<td>72,510</td>
<td>1,144,550</td>
</tr>
</tbody>
</table>

Smith D et al, CROI 2018, Abstract 86
Prevalence of PrEP Users per 100,000 Population
Q2 2017

PrEPVu: Matching PrEP Uptake to PrEP Need

PrEP Users per 100,000 Population
- [3.5 - 7.8]
- [7.8 - 9.7]
- [9.7 - 15.9]
- [15.9 - 20.7]
- [20.7 - 205.5]

PrEP-to-Need Ratio (PnR)
Q2 2017

PrEP Users per New HIV Diagnoses
- [0.5 - 0.9]
- [0.9 - 1.2]
- [1.2 - 1.4]
- [1.4 - 2.5]
- [2.5 - 6.6]
Frequency of any bacterial STI infection, by HIV status and PrEP Use, among Male Patients, Fenway Health

Mayer, OFID, 2017
**PrEP as a gateway to care: Fenway Health**

<table>
<thead>
<tr>
<th>Service</th>
<th>Adjusted Prevalence Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu vaccination</td>
<td>1.57 (1.47-1.67)</td>
</tr>
<tr>
<td>Tobacco screening</td>
<td>1.13 (1.09-1.16)</td>
</tr>
<tr>
<td>Depression screening</td>
<td>1.18 (1.15-1.22)</td>
</tr>
<tr>
<td>Hemoglobin A1c or glucose testing</td>
<td>1.83 (1.75-1.92)</td>
</tr>
<tr>
<td>Hemoglobin A1c testing</td>
<td>0.89 (0.79-1.01)</td>
</tr>
<tr>
<td>Glucose testing</td>
<td>2.03 (1.93-2.14)</td>
</tr>
</tbody>
</table>

Prevalence ratios obtained from Poisson models with generalized estimating equations. Adjusted models included age, gender, race/ethnicity, insurance type, and year, with diabetes, hypertension, and overweight/obesity additionally included in models for hemoglobin A1c and glucose testing.

Marcus et al., CROI, 2018; AJPH, in press
Purview paradox

HIV providers: 1\textsuperscript{0} care providers should prescribe PrEP

Primary care providers: PrEP is for specialists

Krakower, AIDS and Behavior, 2014
Using EHR data to identify PrEP candidates: patients with incident HIV (cases) and patients without HIV (controls)
8,414 (1.1%) of patients in the HMO population had HIV prediction scores above an inflection point in the distribution of scores.

Atrius Health
~800,000 patients
885 HIV-infected patients
249 currently receiving PrEP

8,414 Potential New Candidates for PrEP

Very Low Risk Low Risk High Risk

D Krakower, ID Week, 2016; CROI, 2018
New technologies and TasP/PrEP engagement

- ↑ treatment adherence with text messaging (Lester, Lancet, 2010)
- Daily SMS texting was used to supplement a nurse-delivered PrEP intervention (Safren/Mayer)
- Counseling augmented by electronic diary was associated with ↑ adherence (Amico/Hosek)
- Feedback on drug levels been studied as adjunct to counseling (Landovitz)
- SexPro and MyChoices Apps being developed for young MSM
1) Overencapsulation of Truvada with a gel capsule with integrated radiofrequency emitter creates a "digital pill" (eTectRx).

2) Digital pill is ingested, stomach contents dissolve gel capsule, chloride ion gradient in stomach activates radiofrequency emitter (6ft radius), 30min emission life.

3) Ingestion event recorded by a wearable reader. Data displayed on companion smartphone app.
How to improve chemoprophylaxis effectiveness?

New oral PrEP drugs and dosing strategies

Vaginal & Rectal Microbicides

Intravaginal rings (Dapivirine, Tenofovir) +/- Contraception

Injectables: ARVs and mAbs (Cabotegravir, VRC01)

Novel adherence strategies

Alternative delivery systems and formulations

The Future
Preference for injectable PrEP (vs. daily pill) (Biello, AIDS Behav, 2017)

<table>
<thead>
<tr>
<th>Measure</th>
<th>aOR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-21</td>
<td>1.71 (1.05, 2.79)</td>
<td>0.031</td>
</tr>
<tr>
<td>22-25</td>
<td>1.71 (1.14, 2.55)</td>
<td>0.010</td>
</tr>
<tr>
<td>26-29</td>
<td>1.97 (1.33, 2.93)</td>
<td>0.001</td>
</tr>
<tr>
<td>30-39</td>
<td>1.94 (1.41, 2.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>40-49</td>
<td>1.11 (0.81, 1.51)</td>
<td>0.528</td>
</tr>
<tr>
<td>50+</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.58 (1.17, 2.12)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.45 (1.00, 2.12)</td>
<td>0.053</td>
</tr>
<tr>
<td>Asian/PI</td>
<td>1.18 (0.71, 1.96)</td>
<td>0.513</td>
</tr>
<tr>
<td>Multiracial</td>
<td>1.03 (0.67, 1.57)</td>
<td>0.906</td>
</tr>
<tr>
<td>Other</td>
<td>1.12 (0.46, 2.73)</td>
<td>0.801</td>
</tr>
<tr>
<td>Condomless anal sex acts, past 3 mos.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.11 (0.78, 1.57)</td>
<td>0.559</td>
</tr>
<tr>
<td>2+</td>
<td>1.52 (1.21, 1.91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oral PrEP experienced</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.39 (1.02, 1.89)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

- Preference for injectable PrEP:
  - 47.2% prefer injectable PrEP
  - 16.8% prefer a daily pill
  - 36.0% were unsure

- Difficulty to take injectable PrEP:
  - 47.0% indicated that injectable PrEP would be easier to take as prescribed
Focus Group Results (Biello, Arch Sex Behav, 2017)

- Barriers to PrEP
  - Stigma
  - Lack of knowledge/narrow targeting
  - Preferences for injectables
  - Depend on prior PrEP experience
  - Ppl with adherence difficulties and/or more frequent sex
  - Concerns about injectables
    - Frequent visits, missed injections
    - Length of side effects
    - Injecting foreign substance/mistrust
- Other modalities
  - On-demand method

### Mean (SD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number condomless anal sex partners, past 3 months (range 0-15)</td>
<td>1.6 (2.7)</td>
</tr>
</tbody>
</table>

### Race/Ethnicity

- Latino: 17%
- Black, non-Hispanic: 69%
- White, non-Hispanic: 6%
- Other: 8%

### Male gender identity

- 67%

### Education

- High school diploma or less: 59%
- Past year STI test: 81%
- Past year HIV test: 83%
- Ever PrEP use: 36%

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*We [Black MSM] have too many stories and reasons not to trust vaccines.*  
(Boston participant, PrEP experienced group)

*I honestly don’t want to get an injection if I don’t need it but would still prefer that to the pill.*  
(LA participant, PrEP naïve group)

*I think it would be hard to get every 3 months...It would be better to not have a whole sit-down appointment...If you miss your injection appointment, how many more days of protection would you have? What if I can’t reschedule the appointment in time?*  
(Chicago participant, PrEP experienced group)

*Not everyone is sexually active every single day so not everyone wants to take a pill everyday if they don’t need it. It would be better if you could just take the pill around the time you know you’ll be sexually active.*  
(LA participant, PrEP naïve group)

*I think it would be hard to get every 3 months...It would be better to not have a whole sit-down appointment...Are you going to have side effects the whole 3 months with the injection? Or just the first few days, if any?*  
(Boston participant, PrEP experienced group)
Why the high burden of mental health in HIV?

Mental Disorder

HIV

**Demographic**
- Age
- Gender
- Sexual Orientation
- Ethnicity

**SES**
- Income
- Education
- Housing and Food: Security/Insecurity

**Biological**
- Chronic immune activation and HPA dysregulation
- Other Infections (e.g., HCV)

**Community**
- Density
- Safety / Violence

**Intersecting Stigmas**
- Mental Illness
- HIV
- Gender / Sexual Minority
- Substance Use
- Sex Work

**Environmental**
- Natural Disasters
- War/Conflict
- Climate / Water
- Migration

**Psycho-social**
- Social Support
- Loss / Bereavement
- Trauma
- Gender-based violence
- Fear of illness

**Why the high burden of mental health in HIV?**
Interventions to Increase HIV and BSTI Testing

Test

HIV negative
Risk assessment PrEP, adherence counseling

HIV positive
Positive prevention

Enroll in care
ART initiation
Retain
Adherence to ART

Linkage to care

Maintain viral suppression

Decrease in HIV and BSTI transmission

Address concomitant concerns: depression, substance use, relationship dynamics, structural/social issues, STI

Need to Address more than PrEP (and TasP)
Thank You

Rachel Baggaley  Yannis Mamaletzis
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Ed Boyer        Conall O’Cleirigh
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Peter Chai      Robert Remien
Myron Cohen     Steve Safren
Marcy Gelman    Aaron Siegler
Chris Grasso    Patrick Sullivan
Doug Krakower   NIAID, NIMH, NIDA,
Ken Levine      NICHD, CDC, HRSA,
Julia Marcus    Mass DPH, Gilead,
                Viiv, MAC AIDS
                Foundation