International AIDS Conference
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AETC/Consortium Report Back
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Disclosures

- None
Key topics in HIV Prevention

• U=U (including MSM)
• Disparities in PrEP uptake persist
• Data supporting on-demand PrEP are growing, and some MSM may request on-demand PrEP
  • What are key clinical considerations?
• Update on long-acting PrEP formulations
• Much ado about viral remission
Progress towards the 90-90-90 Targets: Global & SF

Progress towards the 90-90-90 Targets, Global 2016

- 70% [51-84%] of people living with HIV know their status
- 77% [57-89%] of people living with HIV who know their status are on treatment
- 82% [60-89%] of people on treatment are virally suppressed

Countries which have achieved the 90-90-90 targets
Botswana, Cambodia, Denmark, Iceland, Singapore, Sweden, United Kingdom

Progress towards the 90-90-90 Targets, San Francisco 2015

- 93% of people living with HIV know their status (NHBS)
- 79% of people living with HIV who know their status are on treatment (SF cases not known to have moved, lab/chart based)
- 91% of people on treatment are virally suppressed (same subset as previous)

Opposites Attract Study: Treatment as Prevention works for MSM couples

- 358 serodiscordant MSM couples with 591 couple-years of follow-up
- 80% on ART
  - 78% had HIV RNA <200 copies/mL
- 57% reported anal sex with outside partners
- STI prevalence 12%-14%
- No linked HIV transmissions in 17,000 acts of condomless anal intercourse
- >12,000 condomless sex acts when HIV+ partner had UDVL and HIV- partner was not on PrEP
- 3 non linked transmissions emphasize the importance of PrEP

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<table>
<thead>
<tr>
<th>HIV Incidence in Serodiscordant MSM Couples</th>
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<tbody>
<tr>
<td><strong>Number of Linked Transmissions</strong></td>
</tr>
<tr>
<td><strong>(couple-years)</strong></td>
</tr>
<tr>
<td>Overall</td>
</tr>
<tr>
<td>CLAI</td>
</tr>
<tr>
<td>Any</td>
</tr>
<tr>
<td>Insertive</td>
</tr>
<tr>
<td>Receptive</td>
</tr>
<tr>
<td>CLAI, HIV RNA (copies/mL)</td>
</tr>
<tr>
<td>≥200</td>
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<tr>
<td>&lt;200</td>
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- HIV diagnoses among MSM decreased slightly during 2008-2014
  - Significant decrease (▲): white (14 states), 35-44 (23 states), and 45-54 (7 states) years
  - Significant increase (▼): Hispanic/Latino (7 states), black (8 states), 13-24 (16 states), and 25-34 (18 states) years
- Reducing HIV diagnoses will require intervention in many states; focus on young, Black, Latino MSM


Unique PrEP Starts (n=98,732)
Male: 85%
Female: 15%

6.9 times increase 2012 - 2016

Mera R, et al. Poster #WEPEC0919
PrEP Utilization Compared With New HIV Infections

PrEP Use Among Blacks and Hispanics Was Low Relative to the Rate of New HIV Infections


- National on-line sample of MSM from the US (n=4698)
  - Survey posted on 2 popular sexual networking sites (3/2016)
- 75% condomless anal sex ≥2x in 3 months
- 85% had not used PrEP, 22% unaware of PrEP
- Black MSM, less educated MSM, MSM born outside US more likely to cite access concerns
- Older MSM more likely to cite concerns about side effects
- Need to educate at-risk MSM, address access concerns among disproportionately affected groups


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<table>
<thead>
<tr>
<th>Reasons for not Using PrEP Among PrEP-Informed Non-Users (n=2926)</th>
<th>Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerns about Costs</td>
<td>40</td>
</tr>
<tr>
<td>Potential side effects</td>
<td>31</td>
</tr>
<tr>
<td>Potential effects on insurance</td>
<td>20</td>
</tr>
<tr>
<td>Medical provider’s reaction if I asked for it</td>
<td>18</td>
</tr>
<tr>
<td>Reaction of sexual partner</td>
<td>5</td>
</tr>
<tr>
<td>Do not know where to access PrEP</td>
<td>31</td>
</tr>
<tr>
<td>Do not feel at risk</td>
<td>19</td>
</tr>
<tr>
<td>Did not think it would be effective</td>
<td>5</td>
</tr>
</tbody>
</table>
IPERGAY: On-Demand PrEP in MSM v. placebo

✓ 2 tablets 2-24 hours before sex
✓ 1 tablet 24 hours later
✓ 1 tablet 48 hours after sex

97% Relative Reduction (open phase)
NNT to prevent 1 HIV Infection: 18

Median number of sex acts per month: 10
Median number of pills per month: 18
58% diagnosed with STI in open label v. 37% in randomized

Did on-demand PrEP remain effective among participants who had infrequent sexual intercourse and therefore used fewer pills?

Molina Lancet 2017

4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse
On-Demand PrEP in MSM with High Risk and Less Frequent Sexual Intercourse (retrospective, N=269)

• Focused on person time when men used ≤15 pills/month taken “systematically or often” during sex
• Considered variability of sexual activity across the trial and the date determination of a potential infection

These data suggest on-demand PrEP with FTC/TDF may be an alternative to daily PrEP for MSM at high risk of HIV acquisition but with less frequent sexual intercourse

Median number of sex acts/month: 5
Median number of pills per month: 9.5

Does pharmacology support on demand dosing?

Prevent HIV infection by delivering…..

1. the right drug(s)
2. to the right biological site(s)
3. at the right concentration(s)
4. for the right length of time

WHO recommends additional HIV prevention measures should be used for 7 days after starting daily PrEP\(^1\)

- Based on Ipergay dosing strategy 2 pills (2-24 hours apart) for anal sex may be adequate
- Target ratios have been defined for TFV and FTC for adequate mucosal protection\(^2\)

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**The Right Time: Time to maximal protection in mucosal tissues**

**How do you start TDF/FTC?**

![Graph showing maximal protection by dose 2 in RT vs dose 3 in FGT]

The Right Time: **Coverage after an exposure**

*How do you stop TDF/FTC?*

- 2 tablets 2-24 hours before sex
- 1 tablet every day during sexual activity
- 2 tablets after the last sexual intercourse
Does Pharmacology Support On Demand PrEP?

- Yes if…..
  - Drug/metabolite can quickly reach sites of infection
    - mucosal tissues/regional lymph nodes
  - Drug/metabolite achieves potent concentrations
    - above IC50, IC95?
  - Drug/metabolite has long residence time to cover residual virus
    - Otherwise may need to continue dosing

- Caveats
  - Can virus be trafficked to sites of low drug concentrations?
  - Do inflammatory processes overwhelm the activity of standard doses/dose frequencies?
  - Might other sources of pharmacologic variability exist (eg microbiome)?

HPTN 067: Clinical Trial of Non-Daily Use of Oral FTC/TDF for PrEP in MSM in Bangkok and Harlem

Sub-analysis of the ADAPT study in n=178 (Bangkok) and n=179 (Harlem/NYC) MSM

- In NYC MSM, overall coverage of sex acts and PrEP adherence was suboptimal
- For non-daily PrEP in both sites, incomplete coverage of sex acts was mostly related to lack of post-sex dosing

Coverage:
≥1 pill taken in the 4 days before sex
≥1 pill taken in the 24 hours after sex

Clinical Experience with On-Demand PrEP in MSM

<table>
<thead>
<tr>
<th></th>
<th>Number (%) choosing On-Demand</th>
<th>Number of Infections on PrEP</th>
<th>Infection Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>France¹</td>
<td>1581 (57%)</td>
<td>0</td>
<td>0 (0 to 0.0030)</td>
</tr>
<tr>
<td>Montreal²</td>
<td>225 (22%)</td>
<td>0</td>
<td>0 (0 to 0.020)</td>
</tr>
<tr>
<td>Combined observed</td>
<td>1806 (47%)</td>
<td>0</td>
<td>0 (0 to 0.0026)</td>
</tr>
<tr>
<td>Expected if not effective³</td>
<td>1806 (47%)</td>
<td>119</td>
<td>6.6 (0.05 to 0.08)</td>
</tr>
</tbody>
</table>

53% with STIs in 12 months prior to baseline


Significant Differences in Baseline Characteristics Among Daily and On-Demand PrEP Users in the Montreal Study²

<table>
<thead>
<tr>
<th></th>
<th>Daily</th>
<th>On-demand</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>36.7 yrs</td>
<td>39.2 yrs</td>
</tr>
<tr>
<td>Main reason for being on PrEP is HIV+ partner</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td># occasional partners last year (mean)</td>
<td>22.3</td>
<td>14.2</td>
</tr>
</tbody>
</table>

PrEP recommendations in 2017
CDC/FDA: Daily
EACS and France: Daily, and may use on demand for MSM
WHO: Daily is the current recommendation, on demand is safe/effective for MSM

Adapted from Grant R, IAS 2017, Paris, France. Symposium #MOSY0804

bayareaaetc.org
Qualitative substudy of daily v. on-demand demonstration study in Amsterdam: real-world challenges

**Amsterdam PrEP Project (AMPrEP)**
- Demonstration project for HIV-negative MSM and transgender persons
- Choice between daily or on-demand PrEP
- Allowed to switch between dosing regimens

**Choice of PrEP regimen at baseline:**
- 103/376 (27%) participants chose on-demand PrEP

**Switches during follow-up**
- 44 switches to daily PrEP
- 39 switches to on-demand PrEP

**Motives to switch to on-demand PrEP (N=69)**

<table>
<thead>
<tr>
<th>Motive</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Having less sex than anticipated</td>
<td>20 (30%)</td>
</tr>
<tr>
<td>Developing aversion against daily medication</td>
<td>17 (25%)</td>
</tr>
</tbody>
</table>

“*It is still medication, I’d rather not have it in my body if I don’t need it*”

Zimmermann HML on behalf of AMPrEP in H-TEAM. WEAC0106LB
Experiences and perceptions of PrEP in relation to other risk reduction strategies in the PROUD study in London

“Had PEP 4 or 5 times... shameful to ..say ‘I have done it again’”

Condoms
“If it was a one night stand it would be condoms”

Strategic positioning
“I don’t generally bottom outside of a relationship”

Sorting positive
“I only play bareback with undetectable guys”

Sorting negative
“on BBRT... I was only selecting negative”

Ejaculate
“Never been to the position of being a passive receptor of ejaculate”

PEP
“Had PEP 4 or 5 times... shameful to ..say ‘I have done it again’”

“It slightly loosens the boundaries rather than taking them off altogether”

Gafos M. TUAC0105

bayareacpac.org
Practical Considerations of On Demand PrEP (off label use)

Patterns of sex
- Have infrequent (<once/week) sex event
- Ability of sex planning / have control over planning for sex with sexual partners

Pros
- Fewer doses (unclear side effect profile)

Cons
- Need to carry tablets at all times (pre/post-sex dose)
- Complicated regimen (No more than 1 dose in 2 hour window)

Discuss the contexts of risk, on-demand and daily PrEP offer options to decrease risk during periods of higher risk activity. Assess for anxiety or trauma.

Emphasize emergency PEP (28 days) and condoms if missed doses

Continue q3mo HIV and rectal/pharyngeal/urine STD testing

Loss of forgiveness of TDF/FTC with on-demand dosing: consider the implications of switching

NOT INTENDED FOR
- Cis- or trans-women
- Safety (renal/bone) concerns
Key topics in HIV Prevention

• U=U (including MSM)
• Disparities in PrEP uptake persist
• Data supporting on-demand PrEP are growing, and some MSM may request on-demand PrEP
  • What are key clinical considerations?
• Update on long-acting PrEP formulations
• Much ado about viral remission
HPTN 077 - Long acting IM cabotegravir for HIV prevention in men and women: Phase 2a, double-blind, placebo-controlled

- Randomized (3:1), IM cabotegravir 600 mg q8 weeks or 800 mg q12 weeks
- Injection site reactions frequent and usually mild/moderate (88% CAB v. 39% placebo)
  - **1 person** (0.8%) had an injection-related discontinuation
- 1 seroconversion (CAB cohort 1): detected 48 wks after final injection; no CAB detected
- **IM cabotegravir 600 mg q8 weeks (after 4-week loading dose)** consistently met prespecified pharmacokinetic (steady-state) targets for women and men
  - Dose being evaluated in phase 3 efficacy in at-risk individuals

HIV-uninfected men and women at low risk for acquiring HIV infection, ages 18 to 65 (n=199)
HPTN 083: Long-acting CAB-LA N~4500

Blinded Injections & Safety Visits

CAB LA 600 mg IM at Weeks 5, 9, and Q8 Weeks thereafter Plus Daily Oral Placebo for TDF/FTC

Daily Oral TDF/FTC Plus Placebo for CAB LA IM at Weeks 5, 9, and Q8 Weeks thereafter

Key
- Cabotegravir oral
- Cabotegravir Oral placebo
- TDF/FTC oral
- TDF/FTC placebo
- Cabotegravir injection
- Cabotegravir placebo injection
HIV prevention for women: dapivirine vaginal ring

- Open-label extension study (OLE), with no placebo ring
  - HOPE follows ASPIRE
  - DREAM follows the Ring Study
- Both enrolling
- IPM submitted an application to the European Medicines Agency

But a 60% reduction in HIV among women >25 years of age
Dapivirine vaginal ring: Do bacteria associated with BV reduce the genital and plasma concentration of dapivirine?

No dapivirine degradation in the presence of *Gardernella* in vivo

Hillier et al, CROI 2017

Hillier et al, IAS 2017
DISCOVER
Pivotal Study of FTC/TAF vs FTC/TDF for PrEP

Primary Endpoint:
Seroconversion rate/100 p-y

Week 0
n=2500
FTC/TAF (200/25 mg) QD

Week 48
n=2500
FTC/TDF (200/300 mg) QD

Once Daily Treatment
Open-label switch option offered

All participants
MSM or TGW

Eligibility: HIV & HBV negative, eGFR ≥60mL/min, 2+ episodes condomless anal sex (past 12W) OR rectal gonorrhea/chlamydia, syphilis (past 24W)

Sample size: N=5400 to show non-inferiority (FTC/TDF vs FTC/TAF), assumes seroconversion rate for FTC/TDF arm based on iPrEX, PROUD, and IPERGAY

Sites: sexual health clinics, LGBT centers, medical offices (North America, EU)

Now fully enrolled (June 2017)
Prolonged HIV-1 remission after perinatal infection
“The South African Baby”

- Weak HIV-specific T/B cell responses
- 5 HIV DNA copies/ million CD4 T cells
- “Sustained virologic remission” = control viral rebound without eradication of HIV in the absence of ART

Violari/Tiemessen et al, Abstract TUPDB0106LB
Delayed viral rebound after treatment during hyperacute HIV-1 infection

SF patient found to have acute HIV infection while starting PrEP
• Underwent treatment interruption after 34 months of ART
• Latent reservoir size $\approx 200$ cells prior to tx interruption
• $\approx 1\%$ of individuals with a similar HIV burden may achieve lifelong ART-free remission

Henrich/Deeks et al, Abstract TUPDB0103
Key topics in HIV Prevention

• U=U (including MSM)
• Ensure more people of color are offered and retained on PrEP
• Some MSM may request to use on demand PrEP off label: Get curious!
  • Careful identification of ideal patient (low frequency sex, highly planned)
• Trials of longer-acting regimens intended for women and men are underway
• Continue q3 month HIV/STD screening and RAPID ART initiation efforts to identify patients in early infection, decrease reservoir size and increase the possibility for viral remission through future interventions
SF “Ask about PrEP” toolkit

Palm card and poster

Ask about PrEP
Ask your doctor about a daily pill that can protect you and your partners.

Patient educational tool

PrEP Basics

90% effective
PrEP is 90% effective if taken daily. PrEP can be taken even if drinking alcohol or using recreational drugs.

Getting into a routine
- Try to take a pill at the same time each day.
- Consider taking it with a meal to help it not stick.
- Not interested in message reminders? Check out UCHealth.org.

Missed a dose?
Just take the next one. For example, if you usually take a PrEP pill in the morning, but wake up at 1PM that day, it's okay to take 'pill in' and continue with your usual schedule the next day. Don't take 2 pills at a time.

Possible side effects
Sore throat, runny nose, head colds, diarrhea, gas, nausea, indigestion. These symptoms go away within 6-12 months.

FDA has issued a warning about sexual encounters and bone mineral density, which refers to normal side effects of PrEP.

Clinical PrEP Essentials

Efficacy key messages:
- PrEP is highly effective for preventing HIV infection when taken daily.
- Full protection after 7 days doses for rectal sex and after 20 daily doses for vaginal sex.
- PrEP does not prevent GC/CT/syphilis/gential warts/HSV/HCV.

Side Effects:
- 1 in 10 may have GI side effects (N/V/abdominal pain); usually resolves by month 1.
- 1 in 200 may have renal dysfunction (typically reversible if d/c PrEP).
- 1% average loss of bone mineral density; reversible if d/c PrEP.

Recommended Lab Screening & Visits:

Initial Labs:
- HIV Ag/Ab (4th gen), HIV RNA (if positive); HBSAg (if non-immune); HCV Ab, ALT, Cr, 3 site GC/CT, RPR, Consider: Ureap, HAV, HBV, HPV vaccines.
- Week 1: Call, check if prescription was filled, adherence, and insurance copy.
- Month 1: If no HIV RNA test at screening, check HIV Ag/Ab (4th gen), Adherence check.
- Q3 Months: HIV Ag/Ab, Cr, GC/CT (3 sites), RPR, check adherence & PrEP indications.

Need Help? U.S. PrEPline, 855-448-7777
Created by: Lauren Wolchok & Robert Grant

Your Prescription

Filling your prescription:
- If you are given a paper prescription, you will need to take it to a pharmacy to fill your medication.
- Duties are not always available. Contact your pharmacy before you go on vacation or if you don’t have a fax.
- Medication by phone or via healthcare provider and fill their prescription that they meet anesthetic with.
- Don’t use on medication.

Cost
- PrEP is having insurance paying them. All are excellence programs that help other to stick.
- For help, contact the PrEPline at managed at (855) 448-7777.

Staying Protected

Lab testing:
- Testing (TST) is only available in Los Angeles County.
- TST can test for HIV and STIs.
- You will also get tested for HIV and STIs.

Clean and healthy in 6 months.

Stopping PrEP

Process to stop PrEP, talk to healthcare provider about using other PrEP options. These have some side effects while not taking PrEP and can be used for extended periods.

Re-starting PrEP
- PrEP is stopped for more than 7 days.

A high-performance test that can be used to treat PrEP in the future.

 providers
- darpun.sachdev@sfdph.org

Provider pocket card

Tailored PrEP education for providers

bayareaaetc.org

AETC Pacific
Bay Area | North Coast