Pre-Exposure Prophylaxis (PrEP): Best Practices for Pharmacists

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Learning Objectives

1. Discuss guidelines on the use of PrEP to prevent HIV infection
2. Describe the pharmacist’s and pharmacy staff’s role in HIV PrEP
3. Counsel patients on the appropriate use of Truvada for HIV prevention
Disclosures

Dr. Kanmaz has no conflicts of interest to disclose
Poll Question

I have been directly involved in either prescribing, dispensing or counseling patients on PrEP?

1. Yes
2. No
Poll Question

How would you rate your knowledge of PrEP?

1. I do not know anything about PrEP
2. I know what PrEP is but that is all
3. I have some baseline knowledge of PrEP
4. I know a lot about PrEP
5. I am an expert on PrEP
HIV TRANSMISSION
Infectious Body Fluids

HIV can be transmitted from an infected person to another through...

Blood

Semen

Breast Milk

Vaginal Secretions

Other fluids where HIV is present

Blood contains the highest concentration of the virus, followed closely by semen and then vaginal fluids.

Blood contains the highest concentration of the virus, followed closely by semen and then vaginal fluids.
Routes of HIV Transmission

**Needles**
- Injection Drug Use
- Tatooing
- Body Piercing

**Sexual**
- Anal
- Vaginal
- Oral

**Razors & Toothbrushes**
- When blood is present

**Perinatal**
- Mother to baby
### Exposure Type & Estimated Risk

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Estimated Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle-Sharing</td>
<td>0.63% (1/150)</td>
</tr>
<tr>
<td>Receptive Anal Intercourse</td>
<td>0.5% (1/200) – 3% (6/200)</td>
</tr>
<tr>
<td>Receptive Vaginal Intercourse</td>
<td>0.1% (1/1000)</td>
</tr>
<tr>
<td>Insertive Anal Intercourse</td>
<td>0.065 (1/1500)</td>
</tr>
<tr>
<td>Insertive Vaginal Intercourse</td>
<td>0.05% (1/2000)</td>
</tr>
<tr>
<td>Oral Sex with Ejaculation</td>
<td>Conflicting data, but felt to be low-risk. PEP recommended for receiver.</td>
</tr>
</tbody>
</table>

HIV DIAGNOSES IN THE US
HIV Transmission Statistics in the US

Approximately 40,000 in US diagnosed in 2016

1 in 99 Americans will be diagnosed in their lifetime

Young MSMs at greatest risk

Improvement from 1 in 78 (2004-2005)

HIGHEST STATE RISK*
DC 1 in 13
MD 1 in 49
GA 1 in 51
FL 1 in 54
LA 1 in 56
NY 1 in 69
TX 1 in 81
NJ 1 in 84
MS 1 in 85
SC 1 in 86
NC 1 in 93
DE 1 in 96
AL 1 in 97

Rate per 100,000 among selected population

Note: HIV data for the year 2016 are preliminary and based on 6 months reporting delay. Therefore, trend data should be based on data through the year 2015 to allow sufficient time (at least 12 months) for reporting of case information to accurately assess trends.
~70% of new infections occurred in MSM
New HIV Infections in MSM 2008-2014

- CDC - National HIV Surveillance System

HIV Diagnoses In Gay & Bisexual Men
By Age and Race/Ethnicity in the US and 6 Dependent Areas 2016

https://www.cdc.gov/hiv/group/msm/index.html

Subpopulations representing 2% or less of HIV diagnoses among gay and bisexual men are not reflected in this chart.

People living in the South and Northeast US more likely to be diagnosed with HIV vs other Americans

- Highest risk in Washington, DC (1 in 13) and the lowest risk in North Dakota (1 in 670)
How Many Can Benefit from PrEP in the US?

1.2 million adults 18-59 yo

- 400,000 sexually active MSMs
- 600,000 sexually active heterosexuals
- 200,000 injection drug users
How Many Are Actually Using PrEP?

- National electronic database evaluated >80% of pharmacies
- 98,732 individuals started PrEP since 2012
- 36,732 individuals started PrEP in 2016 alone

- Highest rates in those >25y
- Proportion of use in women continues to decline

Eliminating HIV Transmission

• HIV Testing
• Pre-Exposure Prophylaxis (PrEP)
• Post-Exposure Prophylaxis (PEP)
• Treatment as Prevention (TasP)
• Consistent Condom Use
• Access to sterile needles and syringes
Dear Colleagues:

Though I usually cover two topics each month, I have chosen to focus on just one for my September letter. The reason for this decision is to ensure that all practitioners are aware of recent significant scientific developments and publications which have a direct impact on one of our most important initiatives: ending the AIDS epidemic in New York State. These developments address the concept of Treatment as Prevention (TasP), which the broader HIV-affected community refers to as Undetectable=Untransmittable, or U=U. There is now evidence-based confirmation that the risk of HIV transmission from a person living with HIV who is on Antiretroviral Therapy (ART), and has achieved an undetectable viral load in their blood for at least 6 months, is negligible. (Negligible is defined as: so small or unimportant as to be not worth considering; insignificant.)¹

As many of you know, for more than a decade clinical trials and cohort studies have indicated that adherence to effective ART reduces the risk of HIV transmission. Today, with immediate ART treatment recommended for all individuals living with HIV, TasP has become the accepted strategy for reducing new infections. Cumulative, evidence-based scientific data supporting the concept of U=U has confirmed the previous epidemiological conclusion posited in 2008: effective antiretroviral therapy blocks HIV sexual transmission.²
HIV PREP GUIDELINES
US PrEP Guidelines

• CDC US Public Health Service PrEP guidelines updated in 2017[1]
  – Reviews clinical trials on PrEP in specific populations
  – Designed to help providers make decisions about PrEP use
  – PrEP indicated in adults at substantial risk of acquiring HIV
  – Includes clinical eligibility, prescribing information, and other services to support PrEP care

• FDA approved Tenofovir Disoproxil Fumarate/Emtricitabine (Truvada) PrEP for adolescents ≥35 kg in 2018
  – Indications and follow-up are the same as for adults
  – Adolescent use will be incorporated into next update

Pre-Exposure Prophylaxis

• What is PrEP?
  – When people at very high risk for HIV take HIV medicines daily to lower their chances of getting infected

• Truvada
  – Tenofovir Disoproxil Fumarate (TDF) 300 mg
    Emtricitabine (FTC) 200 mg
  – One tablet taken by mouth daily
  – Only FDA-approved antiretroviral for PrEP

• Tenofovir Disoproxil Fumarate (TDF) 300 mg alone can be used in PWID and heterosexual men and women as an alternative

# Candidates for PrEP

<table>
<thead>
<tr>
<th>MSM</th>
<th>Heterosexual Women &amp; Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ sexual partner</td>
<td>HIV+ sexual partner</td>
<td>HIV+ injecting partner</td>
</tr>
<tr>
<td>Recent bacterial STD</td>
<td>Recent bacterial STD</td>
<td>Share injection equipment</td>
</tr>
<tr>
<td>High # of sex partners</td>
<td>High # of sex partners</td>
<td></td>
</tr>
<tr>
<td>History of inconsistent or no condom use</td>
<td>History of inconsistent or no condom use</td>
<td></td>
</tr>
<tr>
<td>Commercial sex work</td>
<td>Commercial sex work</td>
<td></td>
</tr>
<tr>
<td></td>
<td>In high-prevalence area</td>
<td></td>
</tr>
</tbody>
</table>

- People who use stimulant drugs associated with high-risk behaviors (methamphetamine)
- People prescribed multiple courses of non-occupational post-exposure prophylaxis (nPEP)

How Long Does it Take to Achieve Protection?

- Rectal Tissue – 7 days
- Cervicovaginal Tissue – 20 days
- Blood – 20 days

Eligibility Criteria

- Documented negative HIV test
- No signs/symptoms of acute HIV infection
- Creatinine clearance $\geq 60$ mL/min
- Weight $\geq 35$ kg
- No contraindicated medications
- Documented hepatitis B virus infection and vaccination status

Prescription and Follow-Up

<table>
<thead>
<tr>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>- <strong>Truvada</strong>: Tenofovir 300mg/Emtricitabine 200 mg once daily by mouth; No more than 90-day supply</td>
</tr>
<tr>
<td>- Follow-up visits at least every 3 months</td>
</tr>
<tr>
<td>- HIV test, adherence counseling, behavioral risk reduction support, side effect assessment, STI assessment</td>
</tr>
<tr>
<td>- At 3 months and every 6 months thereafter assess renal function</td>
</tr>
<tr>
<td>- Every 3 months, test for bacterial STI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MSM</th>
<th>Heterosexual Women &amp; Men</th>
<th>Injection Drug Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral/Rectal STI Testing</td>
<td>- Pregnancy test every 3 months</td>
<td>Access to clean needles/syringes and drug treatment services</td>
</tr>
</tbody>
</table>
HOW WELL DOES PREP WORK?
# Overall Results of PrEP Trials

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Participants</th>
<th>Medication</th>
<th>mITT efficacy*</th>
<th>Adherence-adjusted efficacy based on TDF detection in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>%</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study</td>
<td>Injecting drug users</td>
<td>TDF</td>
<td>49</td>
<td>(10–72)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/FTC</td>
<td>67</td>
<td>(44–81)</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>HIV discordant couples</td>
<td>TDF</td>
<td>75</td>
<td>(55–87)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/FTC</td>
<td>62</td>
<td>(22–83)</td>
</tr>
<tr>
<td>TDF2</td>
<td>Heterosexually active men &amp; women</td>
<td>TDF/FTC</td>
<td>42</td>
<td>(18–60)</td>
</tr>
<tr>
<td>iPrEx</td>
<td>Men who have sex with men</td>
<td>TDF/FTC</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>Fem-PrEP</td>
<td>Heterosexually active women</td>
<td>TDF/FTC</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>VOICE</td>
<td>Heterosexually active women</td>
<td>TDF</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/FTC</td>
<td>NS</td>
<td>—</td>
</tr>
</tbody>
</table>

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Effectiveness of TDF/FTC PrEP Improves With Adherence

- **VOICE/FEM-PrEP**[^1,^2]
  - Efficacy 0%/6%
  - Adherence 29%/≤37%
- **Partners PrEP[^5]**
  - Efficacy 75%
  - Adherence 81%
- **iPrEx[^3]**
  - Efficacy 44%
  - Adherence 51%
- **TDF2[^4]**
  - Efficacy 62%
  - Adherence 80%
- **PROUD[^6]**
  - Efficacy 86%
  - Adherence ~100%

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

References in slidetext.
## Case Reports of PrEP Failure: HIV Infection Despite High Adherence

<table>
<thead>
<tr>
<th>Patient</th>
<th>PrEP Adherence</th>
<th>Seroconversion</th>
<th>Likely Cause of PrEP Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>43-yr-old MSM[1]</td>
<td>24 mos, supported by pharmacy records, blood concentration analyses, clinical history</td>
<td>Acquired MDR HIV</td>
<td>Exposure to PrEP-resistant, multiclass-resistant HIV strain</td>
</tr>
<tr>
<td>MSM in his 20s[2]</td>
<td>Excellent by self-report, supported by blood and hair concentration analyses</td>
<td>Acquired MDR HIV after 2x condomless insertive anal sex with 2 different partners within 11 wks before diagnosis</td>
<td>Exposure to PrEP-resistant, multiclass-resistant HIV strain</td>
</tr>
<tr>
<td>50-yr-old MSM[3]</td>
<td>Excellent by self report, supported by blood analyses</td>
<td>Acquired wild-type HIV after 2-5 median condomless anal sex partners per day in each mo following PrEP initiation</td>
<td>Chronic rectal inflammation ± trauma</td>
</tr>
<tr>
<td>34-yr-old MSM[4]</td>
<td>Hair sample indicative of high adherence in preceding months</td>
<td>Acquired MDR HIV</td>
<td>Exposure to PrEP-resistant, multiclass-resistant HIV strain</td>
</tr>
<tr>
<td>21 year-old MSM[5]</td>
<td>Excellent by self-report, supported by blood and hair concentration analyses</td>
<td>Acquired MDR HIV</td>
<td>Exposure to FTC-resistant, but TDF-susceptible HIV strain</td>
</tr>
</tbody>
</table>

PrEP is not 100% effective, but it is highly protective; condom use with PrEP optimizes HIV prevention and protects against STIs

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Sharp Increase in STIs

2.3 million cases in 2017 surpasses record set in 2016 by more than 200,000 cases
4th consecutive year

**Gonorrhea**
- Increased 67% (from 333,004 to 555,608 cases)
- Nearly doubled among men (from 169,130 to 322,169)
- Cases in women, up for 3rd year in a row from 197,499 to 232,587

**Primary & Secondary Syphilis**
- Increased 76% (from 17,375 to 30,644 cases)
- MSM made up almost 70% of primary and secondary syphilis cases

**Chlamydia**
- Remained most common condition reported to CDC
- 1.7 million+ cases in 2017, 45% among 15- to 24-year-old females

SAFETY
Side Effects of Truvada

- **Common side effects**: headache, stomach-pain and decreased weight
- **Black Box Warning**: worsening of hepatitis B infection upon discontinuation
- **BMD decreases**: calcium & vitamin D
- **GFR decreases**: not clinically significant
Is TDF/FTC PrEP Safe?

- Meta-analysis of randomized, placebo-controlled PrEP studies demonstrated that the risk of any AE or grade 3/4 AEs is not increased for TDF-based PrEP vs placebo[^1]

- Bone safety: iPrEx bone mineral density substudy[^2;3]
  - High-risk MSM/TGW who received TDF/FTC PO QD PrEP and had dual-energy x-ray absorptiometry assessment (N = 498)
  - Small net decrease in spine and total hip BMD with TDF/FTC vs PBO at Wk 24 (-0.91% and -0.61%, respectively; \( P = .001 \) for both)
  - No difference in fracture rate between groups (\( P = .62 \))
  - BMD lost from hip and spine during TDF/FTC use recovered following discontinuation

PrEP and Renal Safety

- Analysis of eGFR changes with TDF ± FTC PrEP in Partners PrEP (N = 4640)\(^1\)
  
  - Over 36 mos of continuous use, PrEP use did not result in a progressive change in renal function

- Analysis of renal function in iPrEx OLE (N = 220): eGFR decrease to < 70 mL/min more frequent at higher levels of TFV exposure among those with BL eGFR < 90 mL/min or who were older than 40 yrs\(^2\)

THE ROLE OF THE PHARMACIST & PHARMACY STAFF IN PREP
The Pharmacist’s and Pharmacy Staff’s Role in PrEP

- Patient Education
- HIV Testing
- Medication Access
- Gilead Advancing Access Program
  - [https://www.gileadadvancingaccess.com/](https://www.gileadadvancingaccess.com/)
- Adherence Counseling
# PrEP Drug Interactions

<table>
<thead>
<tr>
<th>Medication</th>
<th>Tenofovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir, valacyclovir, cidofovir, ganciclovir, valganciclovir,</td>
<td>• Serum concentrations of these drugs and/or tenofovir may be increased.</td>
</tr>
<tr>
<td>aminoglycosides, high-dose or multiple NSAIDS or other drugs that</td>
<td>• Monitor for dose-related renal toxicities</td>
</tr>
<tr>
<td>reduce renal function or compete for active renal tubular secretion.</td>
<td></td>
</tr>
</tbody>
</table>
You must have a negative HIV test before taking this drug and at least every 3 months while you take it. Tell your doctor if you think you have been exposed to HIV.

Call your doctor right away if you have fever, headache, feel tired, joint or muscle aches, throwing up, loose stools (diarrhea), sore throat, rash, night sweats, or swollen glands.

Call your doctor right away if you had any of these signs within 1 month before you start taking this drug.
Take charge of your health and prevent HIV with PrEP

(tenofovir disoproxil fumarate and emtricitabine)

**PrEP stands for Pre-Exposure Prophylaxis.**

The definition of “prophylaxis” is an action to prevent disease. The goal of PrEP is to prevent HIV infection from taking hold by taking medicine before you are exposed to the virus.

- PrEP is a medicine prescribed to people who do not have HIV infection but are at high risk for getting it.

- PrEP is a combination of two medicines to prevent HIV. It is made up tenofovir disoproxil fumarate and emtricitabine in one pill, which ensures you are getting the right combined daily dose for the medicine to work.

How should this medicine be used?

- You must take one tablet by mouth every day. *With or without food*

- Do not stop taking PrEP without talking to your doctor. When your supply of medicine starts to run low, contact your doctor or pharmacy to get more.

- You will be at higher risk of becoming infected with HIV if you miss multiple doses or stop taking PrEP than if you take it every day.
What should I do if I forget a dose?

- Take the missed dose as soon as you remember it.

  **However, if it is almost time for the next dose, skip the missed dose and continue with your regular dosing schedule.**

- **Do not take a double dose** to make up for a missed one.

- An occasional missed dose will not greatly impact overall effectiveness, but it is important to take the medicine every day. If you miss doses frequently, talk to your doctor.
What side effects can this medication cause?

- Most people do not have side effects while taking PrEP. However, you might experience some of the following when you begin taking the medication:
  - upset stomach
  - vomiting
  - headache
  - loss of appetite

- These side effects usually fade during the first month of taking PrEP. Tell your doctor if any of these symptoms are severe or do not go away.

What other information should I know?

Call your doctor immediately if you have any unusual problems while taking this medication or if you have any of the following:

- fever or chills especially with sore throat, cough, rash or other signs of infection
Take your PrEP medication daily to ensure you are protected

The goal of PrEP is to prevent HIV infection from taking hold if you are exposed to the virus. Taking your PrEP medicine regularly is critical to keep from getting HIV. For PrEP to work, you need to have enough medicine in your body at all times. When you miss doses, you make it harder for the medicine to protect you.

Taking PrEP every day gives you the most protection.

Not taking PrEP regularly greatly lowers your protection against HIV.
Is PrEP all you need?

Even though PrEP is one important tool for protecting yourself from HIV, no method offers 100% protection. While taking your PrEP medicine, you can further reduce your chance of getting HIV by:

- Using condoms during sex
- Cleaning injection equipment if you inject drugs

Plus, while PrEP greatly reduces your risk for contracting HIV, it won’t protect you from other sexually transmitted infections. **Together, these methods offer more complete protection.**

Do not share toothbrushes or razors
Tips to help you take your PrEP

- Match your medicine schedule to your life: add taking your medicines to things you already do each day, like brushing your teeth or eating a meal.

- Try a pill tray with compartments for each day of the week so you can see whether or not you took your pills that day.

- Set the alarm on your clock, watch, or cell phone for the time you take your medicines.

- Use a calendar to check off the days you have taken your medicines, and circle the date of your next medical appointment.

- Download a free app for your phone that can help remind you of your medical appointments and when it’s time to take your medicines. CDC’s “Every Dose, Every Day” app is available for free in the iTunes app store and Google Play.

- Keep a reminder note on a mirror, on your refrigerator, or anywhere else you will see it each day. Put your next appointment card there, too.

CBA CENTER
**PrEP medications are very safe**

Some people in clinical studies of PrEP had early side effects, such as an upset stomach or loss of appetite, but these were mild and usually went away in the first month. Some people also had a mild headache. No serious side effects were observed. You should tell your health care provider if these or other symptoms become severe or do not go away.

**You can get support for taking your medicine**

- Talk to another PrEP user about what works for them.
- Find a PrEP user support group or online forum.
- Ask friends or family members to remind and support you.
- Find a community program that can assist you.
- Use other services provided by pharmacists or social workers if you have access to them.
Truvada Patient Counseling

- **Hepatitis B** has gotten worse when this drug was stopped in some people with hepatitis B. Close follow-up for a few months is needed when therapy is stopped in people who have hepatitis B. Do not stop taking this drug without calling your doctor. Talk with your doctor.
Truvada Patient Counseling

• **Bone problems** like bone pain, soft bones, and thin bones have happened with this drug. This may lead to broken bones. You may need to have a test to check your bones.

• Take calcium and vitamin D as instructed by your doctor.

• Have your urine checked as instructed by your doctor to monitor your **kidney** function.
Truvada Patient Counseling

• Many HIV-1 tests can miss HIV-1 infection in a person who has recently become infected
• You must continue to use safer sex practices. Just taking TRUVADA for PrEP may not keep you from getting HIV
• If you do become HIV-1 positive, you need more medicine than TRUVADA alone to treat HIV-1
Truvada Patient Counseling

• This drug **does not always prevent HIV**. It needs to be used as part of a program that has **other measures** to help prevent HIV. This includes safer sex habits, testing for diseases passed by having sex, and talking with sex partners who have HIV about their HIV treatment. Talk with the doctor for more information.
Box D: Key Components of Medication Adherence Counseling

Establish trust and bidirectional communication

Provide simple explanations and education
- Medication dosage and schedule
- Management of common side effects
- Relationship of adherence to the efficacy of PrEP
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence
- Tailor daily dose to patient’s daily routine
- Identify reminders and devices to minimize forgetting doses
- Identify and address barriers to adherence

Monitor medication adherence in a non-judgmental manner
- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address them
- Assess side effects and plan how to manage them
When to Stop PrEP

- Patient chooses to stop PrEP
- Evidence of HIV infection
- Adverse events
- Chronic non-adherence
Select Ongoing PREP Studies

• Truvada versus Descovy
  – Started September 2016
  – Expected completion 2020
• Cabotegravir injectable
  – HPTN-083 – 4 sites in NYC
  – Expected completion 2021
  – Other studies reported, phase 2 HPTN 077
• Dapivarine vaginal ring
HELPFUL RESOURCES
Resources


National HIV Curriculum – hiv.uw.edu
Learning Objectives

1. Discuss guidelines on the use of PrEP to prevent HIV infection
2. Describe the pharmacist’s role in HIV PrEP
3. Counsel patients on the appropriate use of Truvada for HIV prevention
Questions

Tina J Kanmaz, PharmD, AAHIVE

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Learning Collaborative Discussion:

1. Is there a patent demographic that your PrEP program is having a harder time reaching?

2. What barriers are you experiencing with starting patients on PrEP?

3. How well are your patients adhering to PrEP and associated monitoring/follow-up?

4. What resources are needed to increase awareness and use of PrEP?
Back-Up Slides
Same-Day PrEP Initiation at Drop-in STD Clinic

• Prospective study of same-day PrEP initiation for adults meeting CDC guidelines for HIV PrEP and receiving care at Denver Metro Health Clinic, a drop-in STD clinic offering integrated low-/no-cost services
  – STD clinic provider prescribed 30-day FTC/TDF PrEP (no refills), provided counseling, ordered baseline labs
  – PrEP navigator/study coordinator scheduled 1-mo f/u at participating clinic, provided counseling, addressed financial assistance/coverage
  – On-site pharmacy dispensed free FTC/TDF PrEP, provided counseling

• Same-day PrEP initiated in 100 patients during current analysis time period
  – Of those 100, 78 attended ≥ 1 PrEP f/u appt and 57 attended ≥ 2 PrEP f/u appts
  – No AEs or abnormal labs


Slide credit: clinicaloptions.com
Same-Day PrEP Initiation: Baseline Characteristics and Predictors for Attending ≥ 1 F/U Appointment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (N = 100)</th>
<th>Logistic Regression of Predictors for Attending ≥ 1 Follow-up Appointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yrs (IQR)</td>
<td>28 (25-33)</td>
<td></td>
</tr>
<tr>
<td>Male sex, %</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Hispanic (any race)</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Median annual income, $ (IQR)</td>
<td>24,000 (14,400-38,000)</td>
<td></td>
</tr>
<tr>
<td>Any type of health insurance, %</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Has PCP, %</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>GC/CT/syphilis in past 180 days, %</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

- Each additional increase in annual income of $10,000 associated with 1.68-fold increase in odds of attending ≥ 1 f/u appt after adjusting for age, health insurance, and race/ethnicity ($P = .02$)

Meta-analysis of Safety in Randomized Placebo-Controlled TDF-Based PrEP Trials

- 13 randomized placebo-controlled FTC/TDF or TDF PrEP trials (N = 15,678; 22,250 person-yrs of f/u)
  - 7 in MSM, 3 in women, 2 in serodiscordant couples, 1 in PWID; 3 of TDF alone, 1 of on-demand PrEP in MSM
  - Trials with >1 yr follow-up showed significantly lower serious AE risk with PrEP vs placebo (RD: -0.01%; P = 0.02)

<table>
<thead>
<tr>
<th>Safety Outcome, %</th>
<th>PrEP</th>
<th>Control</th>
<th>Pooled Risk Difference, %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3/4 AEs</td>
<td>17.4</td>
<td>16.8</td>
<td>0</td>
<td>.53</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>9.4</td>
<td>10.1</td>
<td>0</td>
<td>.80</td>
</tr>
<tr>
<td>Bone fractures</td>
<td>3.7</td>
<td>3.3</td>
<td>0</td>
<td>.50</td>
</tr>
<tr>
<td>Grade 3+ SCr elevations</td>
<td>0.1</td>
<td>0.1</td>
<td>0</td>
<td>.68</td>
</tr>
<tr>
<td>Grade 1-4 SCr elevations</td>
<td>4.3</td>
<td>2.3</td>
<td>2</td>
<td>.04</td>
</tr>
</tbody>
</table>

On Demand PrEP Previnir Study

- 1435 at-risk, HIV-negative individuals, nearly all MSM, in Paris region
- At enrollment, 44% of participants used PrEP daily and 53% used it on demand
- 1628 people have enrolled, almost all of whom (98.8%) are men who have sex with men
  - 12 heterosexual men and women as well as 8 transgender people have enrolled
- Double dose of PrEP (two pills) from 2-24 hours before anticipated sex, and then, if sex happens, additional pills 24 hours and 48 hours after the double dose
- In the event of sex on several days in a row, one pill should be taken each day until 48 hours after the last sexual intercourse
- Zero Infections in both arms
- Condoms have been used during 22% and 19% of sexual acts, in those using on-demand and daily PrEP, respectively

OnDemand PrEP, AKA 2-1-1

- 2-1-1 regimen achieved target exposures of tenofovir diphosphate and emtricitabine triphosphate in colorectal tissue at the time of coitus in 81% and 98% of the population when administered 2 and 24 hours before coitus,
- If intercourse is planned, the first (double) dose of PrEP should be taken closer to the 24-hour precoital time
- 2 doses with food 2 to 24 hours before sex, 1 dose 24 hours after the first (double) dose, and 1 dose 24 hours later (“2-1-1” dosing). For consecutive sexual contacts, men were instructed to take 1 pill per day until 2 days after the last sexual encounter.
- ONLY DATA IN MSM!

### PEP Guidelines, April 2016, Regimens

**Adults with Normal Renal Function**

<table>
<thead>
<tr>
<th>Age</th>
<th>Preferred/Alternative</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents aged ≥ 13 years, including pregnant women, with normal renal function (creatinine clearance ≥ 60 mL/min)</td>
<td>Preferred</td>
<td>Tenofovir DF 300 mg and emtricitabine 200 mg (Truvada) once daily with raltegravir 400 mg twice daily or dolutegravir 50 mg once daily</td>
</tr>
<tr>
<td></td>
<td>Alternative</td>
<td>Tenofovir DF 300 mg and emtricitabine 200 mg (Truvada) once daily with darunavir 800 mg once daily and ritonavir 100 mg once daily</td>
</tr>
</tbody>
</table>

# Recommended Indications for PrEP by MSM

<table>
<thead>
<tr>
<th>Males Meeting All of These Criteria</th>
<th>And ≥ 1 of These Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Adult male or adolescent weighing &gt; 35 kg</td>
<td>• Any anal sex without a condom in previous 6 months</td>
</tr>
<tr>
<td>• No acute or established HIV infection</td>
<td>• Bacterial STI (syphilis, gonorrhea, or chlamydia) in previous 6 months</td>
</tr>
<tr>
<td>• Any male sex partner in previous 6 months*</td>
<td></td>
</tr>
<tr>
<td>• Not in monogamous relationship with a recently tested, HIV-negative man</td>
<td></td>
</tr>
</tbody>
</table>

*Assess males who also have sex with women for heterosexual risk.

- CDC summary table also includes a high number of sex partners or commercial sex worker.

### Recommended Indications for PrEP by Heterosexual Women/Men

<table>
<thead>
<tr>
<th>Males &amp; Females Meeting All of These Criteria</th>
<th>And ≥ 1 of These Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Adult or adolescent weighing &gt; 35 kg</td>
<td>▪ Is a male who has sex with both men and women (bisexual)*</td>
</tr>
<tr>
<td>▪ No acute or established HIV infection</td>
<td>▪ Infrequent condom use with ≥ 1 partner(s) with unknown HIV status at substantial risk of HIV infection (PWID or bisexual male)</td>
</tr>
<tr>
<td>▪ Any sex with opposite sex partner in previous 6 months</td>
<td>▪ Is in ongoing relationship with HIV+ partner</td>
</tr>
<tr>
<td>▪ Not in monogamous relationship with a recently tested, HIV-negative partner</td>
<td>▪ Bacterial STI (syphilis, gonorrhea in females or males) in previous 6 months</td>
</tr>
</tbody>
</table>

*Assess males who also have sex with men for MSM risk.

- CDC summary table also includes a high number of sex partners or commercial sex worker

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## Recommended Indications for PrEP by People Who Inject Drugs (PWID)

### PWID Meeting All of These Criteria
- Adult or adolescent weighing > 35 kg
- No acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in the previous 6 months

### And ≥ 1 of These Criteria
- Any sharing of injection or drug preparation equipment in the past 6 months
- Risk of sexual acquisition*
OLE: PrEP Reduces Incidence of HIV in MSM Even With Incomplete Adherence

- Open-label extension of ATN 082, iPrEx, and US Safety Study PrEP trials in HIV-negative MSM and transgender women (N = 1603; 76% receiving daily oral TDF/FTC)[1]

HIV Incidence and Drug Concentrations

<table>
<thead>
<tr>
<th>TFV-DP in fmol/punch</th>
<th>HIV Incidence per 100 Person-Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 LLOQ</td>
<td>5</td>
</tr>
<tr>
<td>(350)</td>
<td>4</td>
</tr>
<tr>
<td>(500)</td>
<td>3</td>
</tr>
<tr>
<td>(700)</td>
<td>2</td>
</tr>
<tr>
<td>(1000)</td>
<td>1</td>
</tr>
<tr>
<td>(1250)</td>
<td>0</td>
</tr>
<tr>
<td>(1500)</td>
<td>0</td>
</tr>
</tbody>
</table>

Risk reduction, %[2] 95% CI[2]

- 44 -31 to 77
- 84 21 to 99
- 100 86 to 100 (combined)


Slide credit: clinicaloptions.com