HIV Pre-Exposure Prophylaxis (PrEP) Are You Ready?

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Disclosures

- I, May Lau, have the following commercial relationships to disclose:
  - Gilead, stockholder
- I, M. Brett Cooper, have no financial disclosures
- I, Adam Leonard, have no financial disclosures

- We will be discussing off label use of medication
What is PrEP?
Objectives

- Discuss components, safety, and efficacy of Pre-Exposure Prophylaxis (PrEP) to reduce risk of HIV infection
- Review indications for PrEP use to prevent HIV infection
- Prescribe and manage adolescent and young adult patients who are on PrEP
HIV Infections

- Estimated 1.2 million infected with HIV
- In 2015, 40,000 people diagnosed with HIV
- Number of new HIV diagnoses from 2005-2014 decreased by almost 1/5

https://www.cdc.gov/hiv/statistics/overview/ataglance.html
HIV Infections

HIV Diagnoses among MSM age 13-24 by Race/Ethnicity, 2005-2014

- Black/African American
- Hispanic/Latino
- White

Source: Centers for Disease Control and Prevention
## Estimated Percentages with PrEP Indications

<table>
<thead>
<tr>
<th>Transmission risk group</th>
<th>% with PrEP indications*</th>
<th>Estimated no.</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men who have sex with men, aged 18–59 yrs†</td>
<td>24.7</td>
<td>492,000</td>
<td>(212,000–772,000)</td>
</tr>
<tr>
<td>Adults who inject drugs, aged ≥18 yrs§</td>
<td>18.5</td>
<td>115,000</td>
<td>(45,000–185,000)</td>
</tr>
<tr>
<td>Heterosexually active adults, aged 18–59 yrs¶</td>
<td>0.4</td>
<td>624,000</td>
<td>(404,000–846,000)</td>
</tr>
<tr>
<td>Men**</td>
<td>0.2</td>
<td>157,000</td>
<td>(62,000–252,000)</td>
</tr>
<tr>
<td>Women</td>
<td>0.6</td>
<td>468,000</td>
<td>(274,000–662,000)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>—</td>
<td>1,232,000</td>
<td>(661,000–1,803,000)</td>
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</tbody>
</table>
What is PrEP?

- 300 mg tenofovir disoproxil fumarate (TDF) and 200 mg emtricitabine (FTC)
- Approved for patients ≥18 years old
PrEP- TDF

- Prodrug of tenofovir
- Competitive inhibitor of HIV and Hepatitis B virus reverse transcriptase
- Long elimination and intracellular half-life
Tenofovir Alafenamide ≠ PrEP
PrEP - FTC

- Cannot be used alone for HIV treatment
- Inhibits hepatitis B virus replication
  - Increases TDF efficacy in viral suppression
PrEP Efficacy

HIV Prevention Efficacy in relation to Adherence

- Condoms
- PrEP

<table>
<thead>
<tr>
<th>Adherence</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% Adherence (7 out of 7)</td>
<td>99%</td>
</tr>
<tr>
<td>57.14% Adherence (4 out of 7)</td>
<td>96%</td>
</tr>
<tr>
<td>28.57% Adherence (2 out of 7)</td>
<td>76%</td>
</tr>
</tbody>
</table>
Potential PrEP Side Effects or Concerns

- PrEP start-up syndrome
- Renal impairment
- Bone density
- HIV resistance
- Birth or infant outcomes
Candidates for PrEP

- Men who have sex with men
- Heterosexual men and women
- Intravenous drug users
Recommended Indications For PrEP Use By Men who have Sex with Men

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in past 6 months
- Any STI diagnosed or reported in past 6 months
- Is in an ongoing sexual relationship with an HIV-positive male partner
Risk Behavior Assessment for Men Who Have Sex with Men (MSM)

In the past 6 months:

- Have you had sex with men, women, or both?
- (If men or both sexes) How many men have you had sex with?
- How many times did you have receptive anal sex (you were the bottom) with a man who was not wearing a condom?
- How many of your male sex partners were HIV-positive?
- (If any positive) With these HIV-positive male partners, how many times did you have insertive anal sex (you were the top) without you wearing a condom?
- Have you used methamphetamines (such as crystal or speed)?
## MSM Risk Index

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
</table>
| **1** | How old are you today? | If <18 years, score 0  
If 18-28 years, score 8  
If 29-40 years, score 5  
If 41-48 years, score 2  
If 49 years or more, score 0 |
| **2** | In the last 6 months, how many men have you had sex with? | If >10 male partners, score 7  
If 6-10 male partners, score 4  
If 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 without a condom? | If 1 or more times, score 10  
If 0 times, score 0 |
| **4** | In the last 6 months, how many of your male sex partners were HIV-positive? | If >1 positive partner, score 8  
If 1 positive partner, score 4  
If <1 positive partner, score 0 |
| **5** | In the last 6 months, how many times did you have insertive anal sex (you were the top) without a condom with a man who was HIV-positive? | If 5 or more times, score 6  
If 0 times, score 0 |
| **6** | In the last 6 months, have you used methamphetamines such as crystal or speed? | If yes, score 6  
If no, score 0 |

Add down entries in right column to calculate total score

**TOTAL SCORE**
Is she a candidate for PrEP?

Sasha
Cases - Patient 1: Sasha

- Transgender female
  - Age: 17 years old
- Has sex with 6 male partner
- Has receptive anal sex without condom

MSM Risk Index

- Age >18 year old score: 0
- Partners >6 score: 4
- Receptive anal sex score: 10
- Total: 14
Recommended Indications For PrEP Use By Heterosexual Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
Risk Behavior Assessment for Heterosexual Men and Women

In the past 6 months:

- Have you had sex with men, women, or both?
- (If opposite sex or both sexes) How many men/women have you had sex with?
- How many times did you have vaginal or anal sex when neither you nor your partner wore a condom?
- How many of your sex partners were HIV-positive?
- (If any positive) With these HIV-positive partners, how many times did you have vaginal or anal sex without a condom?
Is she a candidate for PrEP?

Avianna
Recommended Indications For PrEP Use By Heterosexual Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following:

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
Cases - Patient 1: Sasha

- Transgender female
- Age: 17 years old
- Risk index of 14

“İ’d like an HIV test today”
HIV Testing Technology

- HIV antibody
- Combined HIV antibody and HIV antigen
- Viral Detection

Sensitivity: ≥99.8%
Specificity: ≥99.8%
Time to Test Positivity
Testing Algorithm

Sasha

- **Subjective**
  - Condomless receptive anal intercourse “about two weeks ago”
  - c/o sore throat, HA, rash, “achy”, night sweats

- **Objective**
  - VS WNL w/ exception of T 101.3 F
  - PE notable for: pharyngeal erythema, tender cervical lymphadenopathy, erythematous macular truncal rash

**What HIV test(s) do you want to order at today’s visit?**
**Other tests?**
Would you prescribe PrEP at this visit?
Sasha

Results

- HIV 1/2 Ag/Ab reactive
- HIV 1/2 differentiation indeterminate
- HIV RNA detected 1,230,546 copies

Assessment

- Acute Retroviral Syndrome / Acute HIV Infection
Linkage to Care

- Important to know local HIV care resources
  - Academic medical centers
  - Ryan White care programs
- Rapid linkage with coordinated services is essential
  - Start ARVs, especially acute infection
  - Goal is undetectable viral load
    - Treatment as Prevention (TasP) highly effective in reducing risk of forward transmission, ~98%
Cases - Patient 2: Avianna

- **Subjective**
  - Last sex “more than a month ago, can’t remember if we used condoms.”
  - Says she’s been feeling tired and sick for the last few days w/ HA, muscle aches and noticed rash “all over”

- **Objective**
  - VSS mild temp elevation 99.8 F
  - PE notable for: diffuse erythematous macular rash, cervical and inguinal lymphadenopathy, and patchy alopecia on eyebrows

What HIV test(s) do you want to order at today’s visit? Other tests?
Avianna

- Labs
  - HIV Ag/Ab
  - +/- HIV RNA
  - Syphilis testing
  - All site GC/CT
  - CBC + platelets
  - Metabolic panel
  - Hepatitis serologies
  - Urinalysis

**Would you prescribe PrEP at this visit?**
Avianna

Results
- HIV 1/2 Ag/Ab negative
- HIV RNA NOT detected
- RPR reactive, titer 1:64
- TPPA reactive

Assessment
- Syphilis
- Increased risk for HIV infection
Initiation

- Rule out HIV infection
- Baseline kidney function
- Hepatitis serology
- STI screening

- Opportunity to engage in primary care

Rx Emtricitabine/Tenofovir Disoproxil Fumarate 200/300 mg 1 pill PO QD
dispense 30 0 Refills
Monitoring

- At least every 3 months to
  - Repeat HIV testing and assess for signs or symptoms of acute infection
  - Repeat pregnancy testing for patients who may become pregnant
  - Provide a prescription or refill authorization of daily TDF/FTC for no more than 90d
  - Assess side effects, adherence, and HIV acquisition risk behaviors
  - Provide support for medication adherence and risk-reduction behaviors
  - Respond to new questions and provide any new information about PrEP use

- At least every 6 months to
  - Monitor eCrCl
  - Conduct STI testing

- At least every 12 months to
  - Evaluate the need to continue PrEP as a component of HIV prevention
Consent / Confidentiality

- All 50 states allow minors access to STI testing and treatment (age varies)
  - 27 allow testing/treatment for HIV, 5 testing only

- Confidentiality is tough to maintain due to insurance policies and EOBs
  - 4 states (CA, MD, OR, WA) allow minors to request confidential EOB from insurance

https://www.guttmacher.org/state-policy/explore/minors-access-sti-services
PrEP is Safe

Is Emtricitabine-Tenofovir Disoproxil Fumarate Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection Safer Than Aspirin?

Noah Kojima¹ and Jeffrey D. Klausner¹,²

Conclusions. We conclude that FTC-TDF for PrEP for HIV infection favorably compares with aspirin in terms of user safety. Although long-term studies are needed, providers should feel reassured about the safety of short- and medium-term PrEP for HIV infection with FTC-TDF.
Counseling

- Condoms, routine STI screening, discuss status w/ partners
- Daily adherence
- Lead time to protective drug level varies by exposure site
  - 7 days rectal exposure
  - ~20 days cervical/vaginal exposure
  - ~20 days blood exposure
  - ~20 days (?) penile exposure
- s/sx acute HIV infection
PrEP Medication Adherence

Achieve maximum prevention benefit

HIV Prevention Efficacy in relation to Adherence

- 100% Adherence (7 out of 7)
  - Condoms: 70%
  - PrEP: 99%
- 57.14% Adherence (4 out of 7)
  - Condoms: 40%
  - PrEP: 96%
- 28.57% Adherence (2 out of 7)
  - Condoms: 20%
  - PrEP: 76%
PrEP Medication Adherence

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
PrEP Medication Adherence

Quarterly visits vs. monthly visits

Access / Insurance

- Varies by private plan / state medi-caid program
- Often not covered for minor patients
- Gilead patient assistance programs (18+)
  - Copay assistance $3,600 annually
  - Access program for uninsured 500 x FPL
- Private foundations
  - Patient Access Network Foundation
  - Patient Advocate Foundation
- Novel local programs
Resources

- USPHS PrEP Clinical Practice Guidelines
- National Clinician Consultation Center
  - PrEP (855) 448-7737 or (855) HIV-PrEP
  - PEP (888) 448-4911
  - HIV/AIDS Management (800) 933-3413
  - http://nccc.ucsf.edu
- San Francisco Health Network PrEP Protocol including AYA section
- Please PrEP Me
  - http://www.pleaseprepme.org
Discussion

What Youth of Color Need:

80% of new HIV cases among young people ages 13-24 occur among youth of color. Young people of color are at higher risk for HIV even when they have the same or fewer risk behaviors as white youth.

- Prevention programs that address cultural needs
- Build their skills of condom use and negotiation
- Normalized widespread, HIV testing
- Full funding for a vaccine, a cure, and a voice in decisions that affect them
- Removal of structural barriers to health, like poverty and racism
- Access to health care, including early detection and treatment of HIV
- National Youth AIDS Awareness Day is April 10, youthaidsday.org
Selected References


“Risk Compensation”

- STI rates rising prior to PrEP
- ~10% MSM who did not engage in CAS before PrEP said they might after PrEP
- Population who may benefit most from PrEP have high baseline STI rate
- No evidence that STIs reduce effectiveness of oral PrEP
- TDF/FTC is also PrEP for HBV and HSV2
  - Partners PrEP: 35% reduction of HSV-2 w/ known HSV-2 infected partner
- Condoms counseling and regular STI screening is integral to PrEP services
  - Early detection and treatment/partner services
- Provider bias perpetuates health disparities
PrEP and Hormonal Contraceptives

- No known drug interactions between TDF/FTC and hormonal birth control
- TDF/FTC is part of a preferred regimen for pregnant women living with HIV
- PrEPception

Pregnancy and breastfeeding are not contraindications to PrEP. Currently, there is no reported increase in congenital anomalies among children born to women exposed to TDF (2.3%) or to emtricitabine (2.4%) during the first trimester. Data from studies of infants born to HIV-infected mothers and exposed to TDF through breast milk suggest limited drug exposure. Condom use should be encouraged in pregnancy because several studies have reported increased incidence of HIV acquisition during pregnancy, which may also lead to increased perinatal transmission.
PEP to PrEP

- Non-occupational Post Exposure Prophylaxis (nPEP)
  - Within 72 hours of possible HIV exposure
  - 3 drug regimen preferred
    - Dual NRTI backbone
    - Integrase inhibitor
    - Often TDF/FTC 200/300 mg with DTG 50 mg PO QD x 28 days
  - Reassess/retest at end of PEP and continue TDF/FTC QD as PrEP

A 3-drug regimen consisting of tenofovir DF 300 mg and fixed dose combination emtricitabine 200 mg (Truvada®) once daily with raltegravir 400 mg twice daily or dolutegravir 50 mg once daily.

https://stacks.cdc.gov/view/cdc/38856
Table 1. Estimated per-act risk for acquiring human immunodeficiency virus (HIV) from an infected source, by exposure act<sup>a</sup>

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>Rate for HIV acquisition per 10,000 exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>9,250</td>
</tr>
<tr>
<td>Needle sharing during injection drug use</td>
<td>63</td>
</tr>
<tr>
<td>Percutaneous (needlestick)</td>
<td>23</td>
</tr>
<tr>
<td>Sexual</td>
<td></td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>138</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>8</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>11</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>4</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>Low</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>Low</td>
</tr>
<tr>
<td>Other&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Biting</td>
<td>Negligible</td>
</tr>
<tr>
<td>Spitting</td>
<td>Negligible</td>
</tr>
<tr>
<td>Throwing body fluids (including semen or saliva)</td>
<td>Negligible</td>
</tr>
<tr>
<td>Sharing sex toys</td>
<td>Negligible</td>
</tr>
</tbody>
</table>


<sup>a</sup> Factors that may increase the risk of HIV transmission include sexually transmitted diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and preexposure prophylaxis. None of these factors are accounted for in the estimates presented in the table.

<sup>b</sup> HIV transmission through these exposure routes is technically possible but unlikely and not well documented.
Event Based Dosing

1st Dose
2 Tablets
Max 24h-Min 2h before 1st sexual relation

1st relation

2nd Dose
1 Tablet

2nd relation

3rd Dose
1 Tablet after last sexual relation

3rd relation

Last relation

4th Dose
1 Tablet

Be sure to take 2 final doses after last sexual relation

Friday
12am 12pm 7pm 12am 1am 3am 12pm
1 dose every 24h +/-2h

Saturday
12pm 7pm 12am 4am 12pm 7pm 12am
1 dose every 24h +/-2h

Sunday
12am 12pm 7pm 12am
1 dose every 24h +/-2h

Monday
7pm 12am