Pre-Exposure Prophylaxis for HIV: The Basics and Beyond

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Disclosure

I have no financial conflicts of interest.
Learning objectives

1. Describe how to prescribe and monitor PrEP and how to counsel patients about its use.
2. Discuss how to incorporate PrEP into a range of clinical settings.
3. Summarize considerations that apply to the use of PrEP in special populations.
I spend most of my time as a(n):

A. Medical clinician
B. Behavioral health clinician
C. Administrator
D. Case manager
E. Public health official
F. Something else
Prescribing and monitoring PrEP
Case 1

- 22-year-old man, generally healthy, who presents for sexually-transmitted infection (STI) screening
- Insertive and receptive anal sex with 3 men in the past year; uses condoms most of the time
- Physical examination normal
- Rectal NAAT positive for *Neisseria gonorrhoeae*

**Questions:** Is he a candidate for PrEP? How do I prescribe and monitor PrEP in this patient?
PrEP Detailing Kit
Talking points with a new patient

- PrEP efficacy and the importance of adherence
- Side effects: GI, kidney, bone
- Risk of HIV drug resistance if he contracts HIV
- Laboratory monitoring schedule
- Time to maximal protection
- PrEP does not protect against other STIs
Does PrEP lead to increased sexual risk behavior?

**PROUD**
- Immediate PrEP
- Deferred PrEP

**Kaiser**
- Unchanged
- Reduced
- Increased


Case 1, continued

- He wants to start PrEP.
- HIV antibody/antigen, hepatitis B surface antigen negative
- Estimated creatinine clearance normal

**Question:** He has a high-deductible insurance policy and is worried about affording PrEP. What are his options?
Paying for PrEP

- Commercial and governmental insurance coverage varies.
- Manufacturer’s assistance program: [www.gileadadvancingaccess.com](http://www.gileadadvancingaccess.com)
- Other assistance programs: [www.copays.org](http://www.copays.org)
- Governmental assistance programs (e.g., PrEPDAP in Massachusetts)
Billing for PrEP

How does post-exposure prophylaxis interface with PrEP?

Post-exposure prophylaxis, also called PrEP, refers to the use of antiretroviral medication for 28 days following a discrete exposure to HIV infection, such as a condomless sexual encounter with a person known to have HIV infection. PrEP must be started within 72 hours of the exposure and consists of three drugs: PEP is recommended for use in the United States include TDF/FTC with efavirenz. PrEP and PEP may interface in two ways:

1. Patients who present seeking PrEP may meet indications for PEP. For example, a male patient seeking PrEP who reports during his initial evaluation that he engaged in condomless and sex with an HIV-infected man one day prior could benefit from PEP before starting PrEP.

2. Patients who present seeking PrEP may be at high, ongoing risk of HIV infection and thus may also benefit from PrEP. In this case, PrEP can be initiated as soon as the 28 day PEP course is completed, assuming the patient remains HIV-uninfected.

Who can prescribe PrEP?

Any licensed medical practitioner can prescribe PrEP. Infectious disease specialization is not required to prescribe or monitor PrEP. PrEP is a function of primary care. Primary care clinicians can play a key role in ending the epidemic by screening patients for eligibility for PrEP and prescribing it when appropriate.

How do I code and bill for PrEP?

ICD-10 codes that can be used for PrEP include Z20.4 (exposure to HIV), Z20.2 (contact with and suspected exposure to infections with a predisposing sexual mode of transmission), and Z78.899 (other long-term (parental) drug therapy). Clinicians can bill for PrEP visits using CPT codes for prevention counseling (for example, 99402 for a 30-minute prevention counseling visit).

Is PrEP affordable?

TDF/FTC is too expensive to buy out of pocket for most patients. Commercial and governmental insurance varies with regard to coverage of PrEP. Currently, the manufacturer of TDF/FTC offers a patient assistance program that covers the cost of the medication for those who are uninsured or underinsured. Patients can access the assistance program by visiting www.gileadassist.com. In addition, many states have developed drug assistance programs for PrEP.
Incorporating PrEP into clinical practice
PrEP program components

1. Identify or recruit patients who may benefit from PrEP
2. Perform initial and follow-up visits
3. Support medication and laboratory adherence
4. Link patients to financial assistance, if needed
Example: IDA clinic at MGH

- HIV/primary care clinic in Boston
  - > 10 HIV providers (MDs)
  - Trainees
- Co-located with a DPH STI clinic
  - 3 nurse practitioners
- Nursing, phlebotomy, and benefits coordinator on-site
PrEP program components

1. Identify or recruit patients who may benefit from PrEP
   - Usually identified as at-risk for HIV by STI NPs; also self-referral, advertising at Pride, partners of HIV-infected patients in the clinic

2. Perform initial and follow-up visits
   - Initial visit/counseling by NP, next visit with MD, then q 3 months with NP alternating with MD

3. Support medication and laboratory adherence
   - Nurse champions

4. Link patients to financial assistance, if needed
   - Meet with benefits coordinator at first visit
Same-day access to PrEP

**Advantages**
- Less loss to follow-up?
- Risk of HIV acquisition while waiting for PrEP

**Disadvantages**
- Logistical challenges
- Lengthy initial visit
Protocol for same-day PrEP

1. NP counsels the patient about PrEP and provides written educational materials
2. STAT serum creatinine, HIV antibody/antigen, hepatitis B surface antigen (+ routine STI screening/treatment, as needed)
3. Meet with benefits coordinator for assistance program enrollment, if needed
4. Prescription for 30 days of TDF-FTC
5. Appointment to see MD within 30 days
PrEP for special populations
Case 1, continued

- The patient initiates PrEP.
- At a 12-month follow-up visit, he remains HIV negative.
- He reports now being in a monogamous relationship with another man who has HIV but is virologically suppressed on ART; they do not use condoms.

Question: Is PrEP worthwhile for him now?
Should I recommend PrEP for serodifferent couples?

No
- HIV treatment prevents transmission.
- It’s not cost-effective.

Yes
- Viral rebound may occur.
- People may not be monogamous.
- A desire for a prevention method patients themselves control.
Viral suppression prevents sexual HIV transmission.

- **Randomized, controlled trial of heterosexual adults:**
  - 1,763 serodifferent couples
  - Immediate ART (versus delayed ART) reduced within-couple HIV transmission by 93%
  - No within-couple transmissions occurred when the index partner was virally suppressed

- **Observational study of heterosexual and MSM adults:**
  - 548 and 340 serodifferent heterosexual and MSM couples, respectively
  - 58,000 episodes of condomless sex over median 1.3 years of follow-up
  - 0 within-couple transmissions
Case 2

- A 36-year-old woman is referred for PrEP.
- Her husband is HIV-infected and is taking ART, though with some lapses in adherence.
- She is sexually active with him; they use condoms most of the time, but she wants PrEP as a back-up form of protection.
- Her only medication is an oral contraceptive.
- She is HIV negative with normal renal function.

**Question**: Is PrEP effective in women?
2 large RCTs did not show a benefit to oral PrEP in women.

- **Population:** 2,120 women in sub-Saharan Africa
- **Intervention:** Oral tenofovir-emtricitabine
- **Results:** No HIV risk reduction with PrEP

**VOICE** (N Engl J Med 2015)
- **Population:** 5,029 women in sub-Saharan Africa
- **Intervention:** Oral tenofovir-emtricitabine, oral/vaginal tenofovir
- **Results:** No HIV risk reduction with PrEP
Differences in study outcomes relate to adherence.

But, biological differences may also play a role.

![Bar Graph](image)

**Time to maximal tissue tenofovir levels with daily use**

- **Cervicovaginal tissue**
- **Rectal tissue**

PrEP does not reduce efficacy of hormonal contraception in women, and vice versa.

Case 2, continued

- She starts PrEP.
- One year later, she remains HIV negative.
- Her husband has been consistently suppressed for 8 months.
- She’s stopped OCPs.
- They want to conceive a child and don’t have access to assisted reproductive technologies.
- They ask if it’s “OK” to have condomless sex in an effort to become pregnant.

**Question:** How would you answer this question?
Can’t HIV Serodiscordant Couples Now Just Have Children the Regular Way?

MMWR just published a paper entitled, *Strategies for Preventing HIV Infection Among HIV-Uninfected Women Attempting Conception with HIV-Infected Men — United States*, and it’s both a welcome and a very strange document indeed.

It’s welcome because it acknowledges that serodiscordant couples may wish to have children without the use of an HIV-negative sperm donor. Advances in HIV prevention mean they can drop their categorical recommendation against insemination with semen from HIV-infected men, one they originally made in 1990.
PrEP may be part of a safe conception strategy.

- No increased birth defects with tenofovir-emtricitabine among women in the Antiretroviral Pregnancy Registry
- No difference in birth outcomes among women receiving PrEP versus placebo in the Partners PrEP study
- However, modeling suggests PrEP adds little, assuming ART and other factors are optimized.

### DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission

#### Panel’s Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples

- For serodiscordant couples who want to conceive, expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple (AIII). It is important to recognize that treatment of the infected partner may not be fully protective against sexual transmission of HIV.

- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).

- For HIV-infected females with HIV-uninfected male partners, the safest conception option is artificial insemination, including the option of self-insemination with a partner’s sperm during the peri-ovulatory period (AIII).

- For HIV-infected men with HIV-uninfected female partners, the use of sperm preparation techniques coupled with either intrauterine insemination or in vitro fertilization should be considered if using donor sperm from an HIV-uninfected male is unacceptable (AII).

- For serodiscordant couples who want to conceive, initiation of antiretroviral therapy (ART) for the HIV-infected partner is recommended (AI for CD4 T-lymphocyte (CD4-cell) count ≤550 cells/mm³, BIII for CD4-cell count >550 cells/mm³). If therapy is initiated, maximal viral suppression is recommended before conception is attempted (AIII).

- Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission (CIII). The utility of PrEP of the uninfected partner when the infected partner is receiving ART has not been studied.

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**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Case 3

- A 17-year-old man presents to the clinic after a sexual partner said he had chlamydia.
- He is sexually active with multiple male partners, rarely using condoms.
- He asks about PrEP, as many of his friends take it.

**Questions:** Would you prescribe PrEP to an adolescent at risk for HIV infection? What special considerations apply to PrEP use in this population?
High HIV risk, suboptimal PrEP adherence

- **15- to 17-year-olds in 6 U.S. cities (ATN 113)**
  - HIV incidence 6.4 per 100 person-years
  - 60% adherent at week 4; 28% at week 48

- **18- to 22-year-olds in 12 U.S. cities (ATN 110)**
  - HIV incidence 3.9 per 100 person-years
  - ~55% adherent at week 4; 34% at week 48

Special considerations for PrEP use in adolescents

- Tenofovir-emtricitabine for PrEP is approved for adults
- Effects on bone mineral density
- Parental consent
- Adherence support (monthly visits?)

Case 4

- 42-year-old transgender women who presents for STI screening
- Engages in sex work; partners are cisgender men
- Diagnosed with syphilis
- Interested in PrEP; concerned about interactions with gender-affirming hormonal therapy (oral estradiol, spironolactone)

**Questions:** Does PrEP interact with gender-affirming hormonal therapy? Are there other special considerations that apply to PrEP use by transgender people?
PrEP works in transgender women, but adherence is crucial.

- No benefit to PrEP in a post-hoc analysis of 339 transgender women, analyzed on an intention-to-treat basis.
- Protective drug levels: 18% of transgender women vs. 36% of MSM
- No infections occurred in transgender women taking 4 doses of PrEP per week.

**Figure 3:** Rate ratios for HIV infection in the iPrEx open-label extension by gender

HIV disproportionately burdens transgender women in the United States.

Several factors are associated with HIV among transgender women.

- Receptive anal intercourse
- Sex work
- Abuse, including anti-transgender violence
- Self-injection of hormones and/or silicone
- Substance abuse
- Depression

Many transgender women are not aware of PrEP.

- **Trans women cohort in San Francisco, 2013:** 14% aware of PrEP
- **Black trans women cohort in New York City, 2012-2015:** ~33% aware of PrEP

- **San Francisco focus group participant:** “To me, this PrEP thing is a white gay man’s thing, okay?”
- **Boston trans activist:** “You never see anything made for trans men. I would immediately be drawn to materials made for me.”

Take-home points

1. Refer to the PrEP Action Kit for information on PrEP prescribing and monitoring, as well as the use of PrEP in special populations.

2. Components of successful PrEP programs: A) identification of patients, 2) plan for clinical monitoring, 3) adherence support, and 4) linkage to financial assistance.
Thank you!

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