NATIONAL LGBT HEALTH EDUCATION CENTER
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NATIONAL CENTER FOR INNOVATION IN HIV CARE

Current Topics in HIV Pre-exposure Prophylaxis

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Objectives

1. Describe basic PrEP management in detail.
2. Apply findings from research to common clinical questions.
3. Summarize considerations involved in creating a clinical PrEP program.

A quick review of PrEP basics

- Indicated for persons with a high HIV risk
- Daily tenofovir-emtricitabine is the only FDA-approved medication
- **Baseline testing**
  - HIV antibody(-antigen)
  - HBsAg
  - Creatinine (to calculate creatinine clearance)
  - Pregnancy test
  - Ask about symptoms of acute HIV infection in the prior 4 weeks
- **Monitoring:**
  - **3 months:** HIV antibody, pregnancy test, creatinine
  - **6 months:** STI screening (syphilis, gonorrhea, chlamydia)

Who is "high risk?"

MSM

Condomless anal sex

Recent sexually-transmitted infection

HIV-infected partner

Heterosexual adults

Condomless sex with a partner who injects drugs or is a bisexual man

HIV-infected partner

Injection drug users

Use of shared injection equipment

Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014. CDC. Available from: http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf

Acute HIV is often a mono-like illness.

Feature	Proportion of patients with acute HIV who have each sign or symptom (%)
Fever	77
Myalgia	52
Rash	51
Headache	47
Pharyngitis	43
Cervical adenopathy	41
Diarrhea	28

Daar ES, Pilcher CD, Hecht FM. Curr Opin HIV AIDS. 2008.

My talking points with a new patient

- PrEP efficacy and importance of adherence
- Periodic HIV testing and creatinine checks are mandatory.
- Side effects: GI, renal, bone
- PrEP does not protect against other sexually transmitted infections.

Common clinical questions

Case 1

- A 35 year-old gay man presents to discuss PrEP.
- While home in Boston, he is rarely sexually active with other men and always uses condoms.
- He is planning to vacation in Spain in one month and anticipates multiple unprotected anal sexual encounters on the trip.
- On a similar trip last year, he contracted Chlamydia urethritis.
- He would like to take PrEP for his upcoming vacation and stop after he returns to Boston.

Would you recommend…

A. Time-limited PrEP for his vacation, with cessation after he returns home?
B. Initiation of PrEP to be continued indefinitely?
C. That he not use PrEP for this purpose?

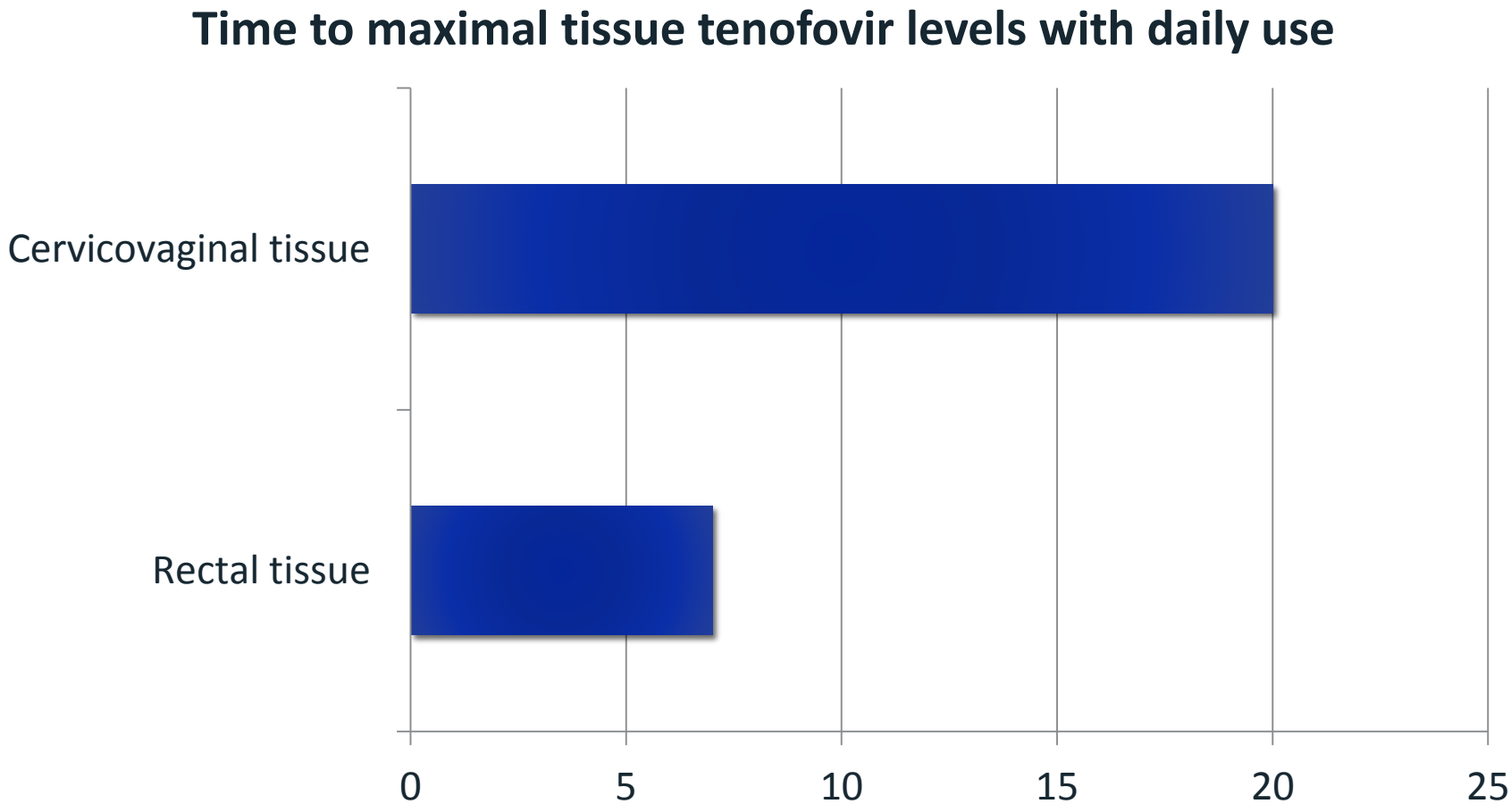
PrEP and "risk vacations"

- PrEP effectiveness has not explicitly been assessed in this situation, but…

- The patient's situation is not materially different than use of PrEP for conception in serodifferent heterosexual couples.
- Suggest:
  - Start PrEP 7-28 days prior to the risk period
  - Take PrEP daily during the risk period
  - Continue PrEP for 28 days after the risk period

Daskalakis D. HIV preexposure prophylaxis in the real world. Top Antivir Med. 2014;22(4):670.

Time to maximal protection may differ by route of HIV exposure.



Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014. CDC. Available from: http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf

Case 2

- A 42-year-old transgender woman presents with rectal pain and discharge.
- She reports having multiple male sexual partners with whom she engages in receptive anal sex, often without condoms.
- Rectal NAAT testing is positive for gonorrhea; she receives ceftriaxone and azithromycin, and her symptoms resolve.
- At follow-up, you suggest she consider PrEP for HIV prevention.
- She has been using an estradiol patch for 5 years and is concerned that PrEP may interact with her hormonal therapy. She also asks if PrEP has been studied in transgender women.

Which is true about PrEP and hormonal therapy?

A. Estradiol lowers the concentrations of tenofovir-emtricitabine, so the dose of PrEP should be doubled.

B. PrEP lowers the concentrations of estrogen in the body, so her estradiol dose may need to be increased.

C. Use of PrEP along with hormonal therapies is contraindicated.

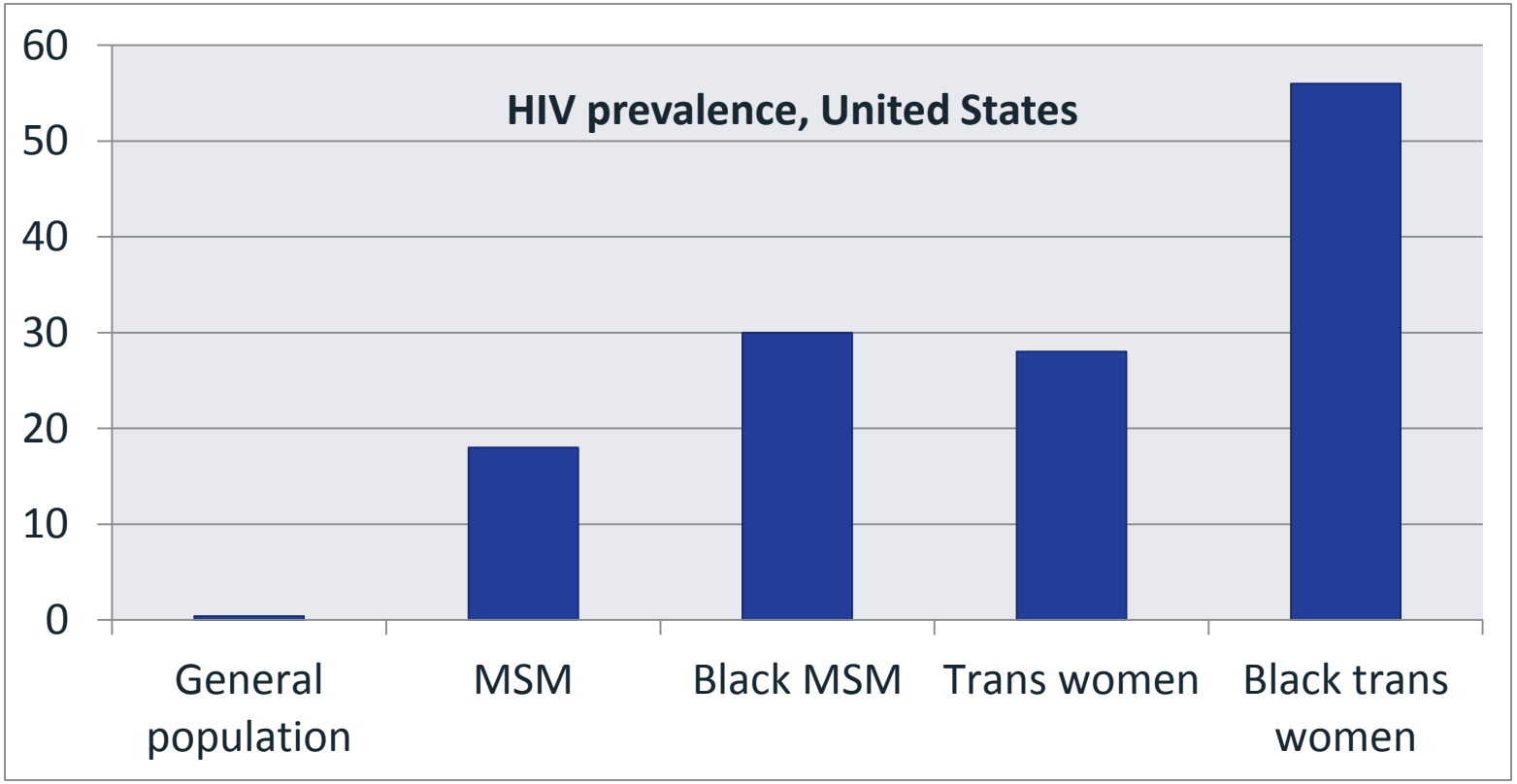
D. There are no known drug interactions between tenofovir-emtricitabine and cross-sex hormonal treatment.

Does PrEP work in transgender women?

- No benefit in 339 transgender women in a post-hoc analysis of iPrEX
- 18% of transgender women had protective drug levels, compared to 36% of MSM.
- No transgender women who contracted HIV had detectable drug levels at the time of diagnosis.
- 0 infections occurred in transgender women taking 4 or more doses of PrEP per week.
- **Bottom line:** PrEP can work, but adherence is crucial.

Deutsch MB, et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial. Lancet HIV. 2015;2:e512.

HIV disproportionately burdens transgender women.



Herbst JH, et al. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. AIDS Behav. 2008;12(1):1.
Wejnert C, et al. HIV infection and awareness among men who have sex with men – 20 cities, United States, 2008 and 2011. PLoS One. 2013;8(10):e76878.

Case 3

- A 22 year-old bisexual man presents 18 hours after condomless receptive anal sex with another man of unknown HIV status.
- His HIV antibody-antigen test is negative.
- He starts PEP with tenofovir-emtricitabine and dolutegravir.
- This is his third PEP course this year.
- He is interested in taking PrEP after finishing PEP.

Which is true about the transition between PEP and PrEP?

A. After completing 28 days of PEP, the patient should stop all antiretrovirals for 3 months; if HIV testing is negative after 3 months, he can start PrEP.

B. PrEP can be started as soon as the 28 days of PEP are finished.

Case 3, continued

- After completing 28 days of PEP, dolutegravir is stopped, and he continues tenofovir-emtricitabine alone for PrEP.
- HIV testing at 3 months remains negative.
- He calls the clinic 2 months later reporting a sexual exposure to HIV 5 hours prior. He has been taking PrEP as prescribed.

What would you recommend now?

A. Add back dolutegravir for 28 days for PEP; thereafter, continue tenofovir-emtricitabine alone for PrEP.

B. Continue tenofovir-emtricitabine for PrEP.

Case 4

- A 27 year-old man is referred for PrEP.
- He is sexually active with 1 primary and 2 occasional male partners.
- He was treated for secondary syphilis 3 months ago.
- Past medical history includes IgA nephropathy.
- An HIV antibody/antigen test is negative. Serum creatinine is 1.72 (eGFR ~ 40).

What would you recommend for PrEP for this patient?

A. Tenofovir-emtricitabine (TDF-FTC)
B. Tenofovir alafenamide-emtricitabine (TAF-FTC)
C. Maraviroc
D. No PrEP

There is insufficient evidence to recommend TAF for PrEP.

Animal Data

- 12 macaques exposed rectally to SHIV
- 6 animals given PrEP with TAF-FTC were protected.
- 6 control animals became infected.

Human data

- 8 healthy women administered a single dose of TAF
- Drug levels measured in blood and tissue from the cervix, vagina, and rectum
- Tenofovir concentrations were undetectable in 83% of tissue samples.

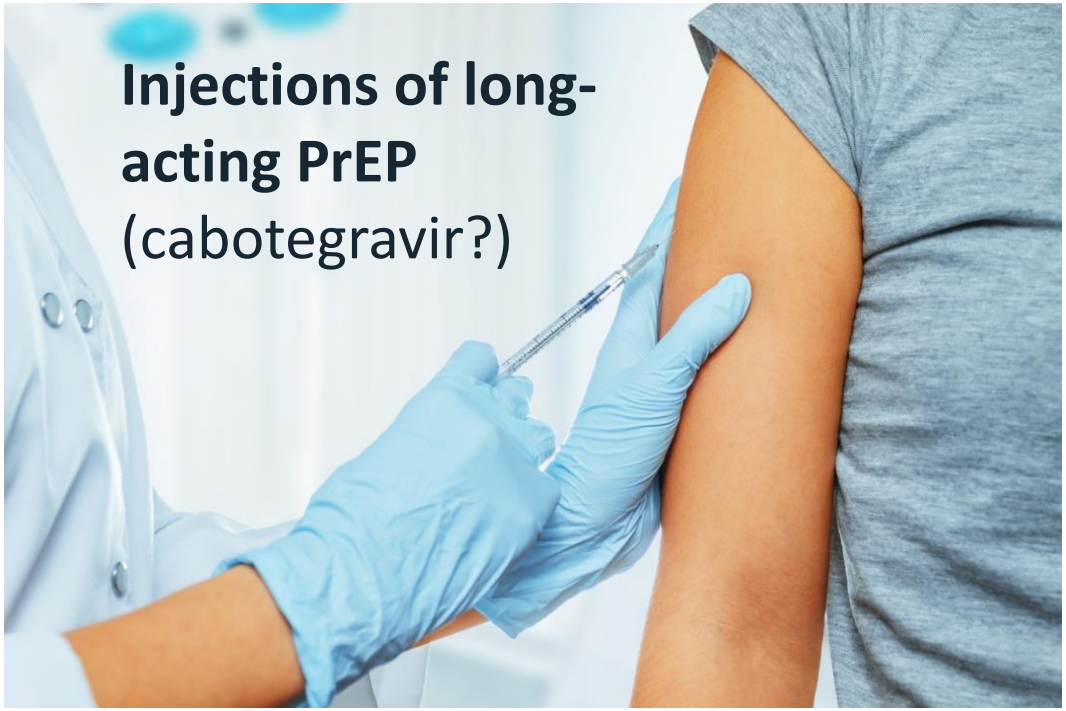
Massud I, et al. Chemoprophylaxis with oral FTC/TAF protects macaques from rectal SHIV infection. CROI 2016. Abstract 107.
Garrett KL, et al. Concentrations of TFV and TFVdp in female mucosal tissues after a single dose of TAF. CROI 2016. Abstract 102LB.

There is insufficient evidence to recommend maraviroc for PrEP.

- **Study:** Phase II study of maraviroc for PrEP
- **Population:** 406 high-risk MSM
- **Intervention:**
  - Maraviroc
  - Maraviroc + emtricitabine
  - Maraviroc + tenofovir
  - Tenofovir + emtricitabine
- **Results:**
  - Maraviroc was safe and well-tolerated.
  - 5 HIV infections occurred, all in maraviroc arms; 4 associated with low or undetectable drug levels.

Gulick R, et al. HPTN 069/ACTG 5305: Phase II study of maraviroc-based regimens for HIV PrEP in MSM. CROI. 2016. Abstract 103.

Topical and injectable formulations are in development.



Case 5

- A 42 year-old man on PrEP presents in follow-up.
- He is in a monogamous relationship with an HIV-infected, male partner who is virologically suppressed on antiretroviral therapy.
- They do not use condoms for sex.
- He asks whether PrEP is needed in this setting.

Would you recommend…

A. PrEP

B. No PrEP

The considerations

PrEP

- Non-monogamy
- Risk of virologic failure in the infected patient
- Recommended by CDC
- Risk tolerance

No PrEP

- Treatment as prevention works
- Not cost-effective

Treatment as prevention works.

- **Study:** PARTNER
- **Population:** 548 heterosexual and 340 MSM serodifferent couples
- **Median follow-up:** 1.3 years
- **Exposure:** 22,000 and 36,000 condomless sex acts for MSM and heterosexual couples, respectively
- **Results:**
  - 0 within-couple HIV transmissions
  - 10 MSM and 1 heterosexual subjects contracted HIV

Rodger AJ, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. JAMA. 2016;316(2):171.

Developing a PrEP program

How will you identify patients who may benefit from PrEP?

- Self-referral
- Partners of HIV-infected patients
- Individuals who test positive for an STI
- Primary care clinician's sexual history
- Nurse-led screening

Who will perform the initial and follow-up visits for PrEP?

- Primary care clinician does all
- Initial visit by a local PrEP expert, follow-up by the primary care clinician
- Follow up visits by nurses, physicians assistants, and/or nurse practitioners
- A clinic devoted to PrEP?

- Are same-day PrEP starts possible?

How will you monitor and support adherence?

- How frequently should patients return for visits?
- Phone check-ins between visits?

How will you assist patients who lack insurance or have high copays?

- Clinician discusses during the visit
- Work with a social worker and/or benefits coordinator
- Collaborate with pharmacists to provide resources to patients if copays are too high

Paying for PrEP

- Coverage by commercial and governmental insurance varies.
- Assistance for insured or uninsured patients is available through the manufacturer: www.gileadadvancingaccess.com
- Assistance for insured patients with high copays or deductibles: www.copays.com (Patient Advocate Foundation)

Take-home points

- Daily tenofovir-emtricitabine substantially reduces the risk of HIV infection in individuals at high risk.
- Adherence is crucial for maximal PrEP efficacy.
- PrEP may not be worthwhile for monogamous serodifferent couples in which the HIV-positive partner is virologically suppressed on ART.
- There are several models of care for PrEP; all must address issues of patient identification, follow-up, and adherence.

Thank you

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