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Case Studies in PrEP Management

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Continuing Medical Education Disclosure

- Program Faculty: Kevin Ard, MD, MPH
- Current Position: Medical Director, The National LGBT Health Education Center, Fenway Health and Massachusetts General Hospital
- Disclosure: No relevant financial relationships. Presentation does not include discussion of off-label products.

This Live activity, Preventing HIV with One Pill a Day: Using PrEP in Clinical Practice, with a beginning date of 04/15/2016, has been reviewed and is acceptable for up to 3.75 Prescribed credit(s) by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.



Objectives

1. Summarize CDC guidelines on HIV pre-exposure prophylaxis
2. Apply key findings from cutting-edge research to real-world clinical scenarios
3. Describe clinical controversies in PrEP management

Case 1

- 24 year-old man referred from STI clinic
- 5 male sexual partners per month; engages in oral and anal sex; condom use inconsistent
- No chronic medical problems
- No prior sexually-transmitted infections
- Physical examination unremarkable
- HIV and STI testing one month ago was negative

Is he a candidate for PrEP?

- **Yes; according to the CDC, MSM who fulfill the following criteria are candidates:**
 - Adult man
 - Without acute or established HIV infection
 - Any male sex partners in past 6 months
 - 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

Pre-exposure prophylaxis for prevention of HIV infection in the United States – 2014. CDC. Available from: www.cdc.gov.



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>

Which tests must be sent before starting PrEP?

A. HIV antibody, hepatitis B surface antibody, urinalysis

B. HIV antibody, hepatitis B surface antigen, serum creatinine

C. HIV RNA, hepatitis B surface antibody, urinalysis

D. HIV RNA, hepatitis B surface antigen, serum creatinine

PrEP prescribing guidelines

- 1. Determine eligibility:** Document negative HIV test and high risk of infection, confirm creatinine clearance > 60 mL/min
- 2. Assess for conditions of concern:** HBsAg/HBsAb for everyone, pregnancy test for fertile women
- 3. Prescribe:** Tenofovir-emtricitabine, 1 tablet by mouth daily (\leq 90-day supply)
- 4. Monitor:** Creatinine, HIV status, pregnancy status every 3 months; STI screening every 6 months; counsel regarding risk reduction

US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014. Available from: www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf.



What would you tell him about side effects?

- Nausea may occur with initiation of tenofovir-emtricitabine; it typically resolves with time.
- Kidney injury occurs rarely (2% in iPrex).
 - Periodic monitoring is obligatory.
 - Abnormalities usually resolve with drug discontinuation.
- A small decrease in bone mineral density may occur; the clinical significance of this is unknown.
- Antiretroviral resistance is unlikely but possible.

How would you counsel him about...

- The length of time on PrEP before he is maximally protected?
 - 7 days, when maximal levels are achieved in rectal tissue?
- If stopping PrEP, how long he should take it beyond his last high-risk sexual encounter?
 - 4 weeks, by analogy to PEP?



My talking points with a new patient

- PrEP efficacy and importance of adherence
- Periodic HIV testing and creatinine checks are mandatory.
- The risk of HIV drug resistance if he/she becomes infected with HIV while on PrEP
- Side effects: GI, renal, bone
- What we think about time to maximal protection, time to continue after last high-risk encounter
- PrEP does not protect against other STIs, except perhaps HSV (Celum, Ann Intern Med, 2014).



Case 2

- 38 year-old man referred after diagnosis of rectal HSV; eager to start PrEP
- 1-2 new sexual encounters per month, mostly with male partners
- Physical examination unremarkable
- HIV antigen/antibody negative, HBsAg negative, creatinine 0.89 (eGFR > 60)
- Unprotected receptive anal sex 1 day ago

How would you manage his recent, high risk exposure in the context of PrEP?

- A. Send an HIV viral load and start PrEP if it's negative
- B. Wait 4 weeks, then recheck an HIV antibody/antigen test and start PrEP if negative
- C. Start PrEP now
- D. Start post-exposure prophylaxis with tenofovir-emtricitabine + dolutegravir, then continue PrEP alone after 28 days

Case 2, follow-up

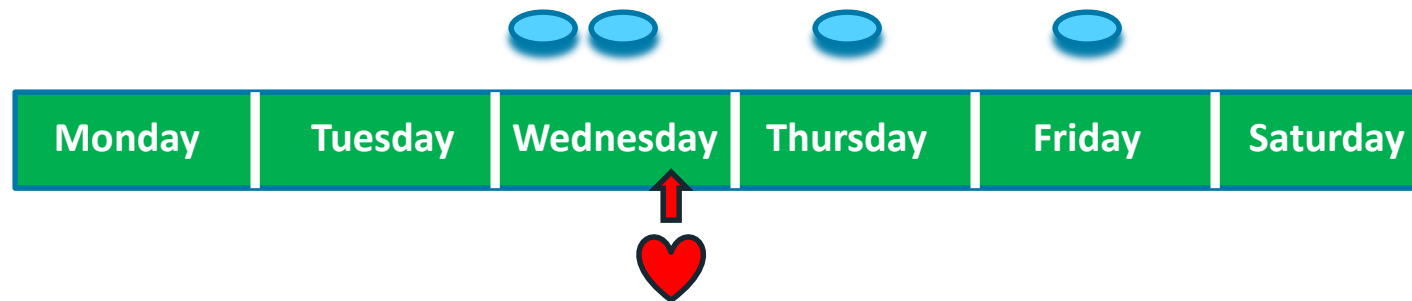
- He starts 3-drug PEP, then continues PrEP alone after 28 days.
- At a 3-month follow-up, his HIV test is negative, and his creatinine is stable.
- His sexual behavior is unchanged.
- He has heard that “on-demand” PrEP (that taken only in the context of sex) can also reduce HIV transmission and wants to stop daily use.

Would you...

- A. Endorse “on-demand” (episodic) PrEP?
- B. Recommend that he continue daily PrEP?

IPEGAY supports “on-demand” PrEP in MSM with frequent sex

- **Population:** 400 MSM reporting unprotected sex with 2 or more partners in the past 6 months
- **Intervention:** Event-driven PrEP versus placebo
- **Results:** 86% reduction in HIV incidence
- **IPEGAY regimen:** 4 pills, 3 doses over 3 days

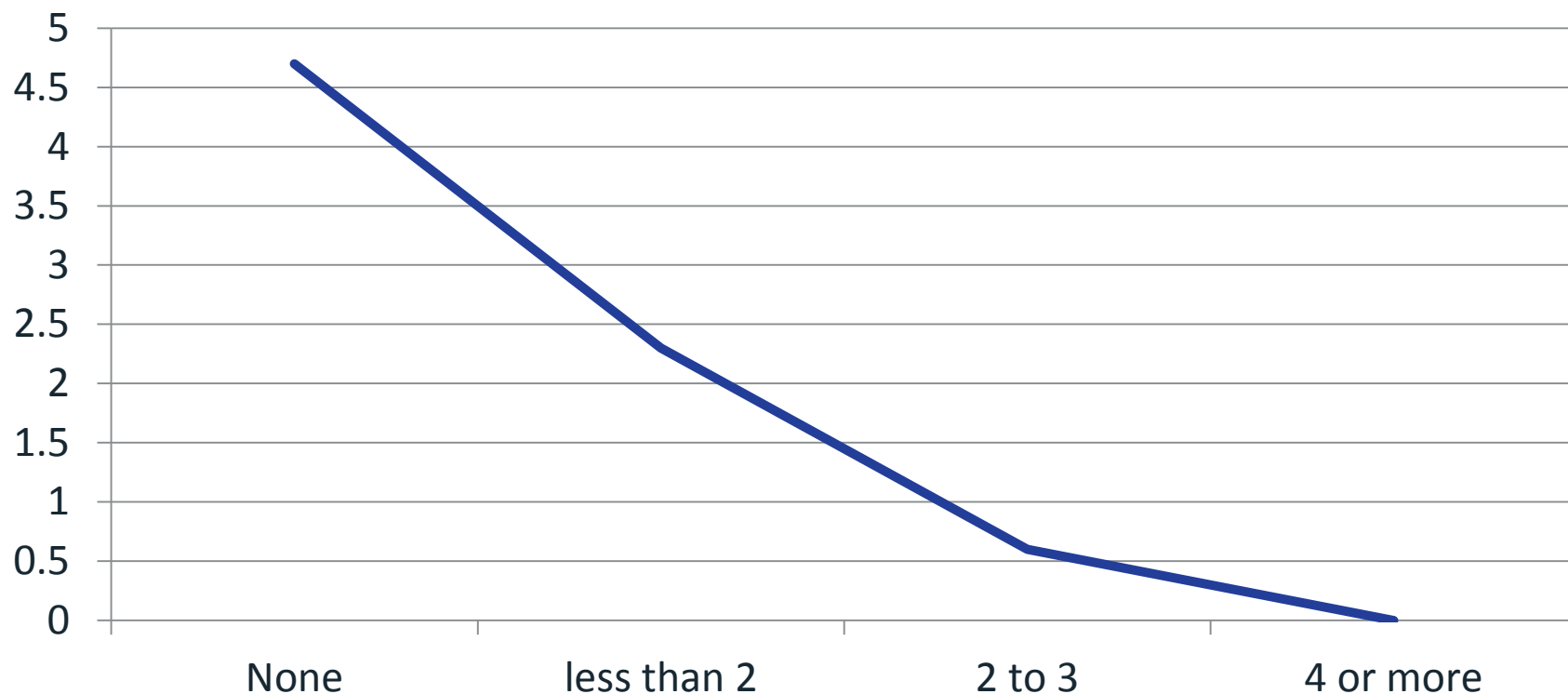


Molina JM, et al. On demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015;373:2237.



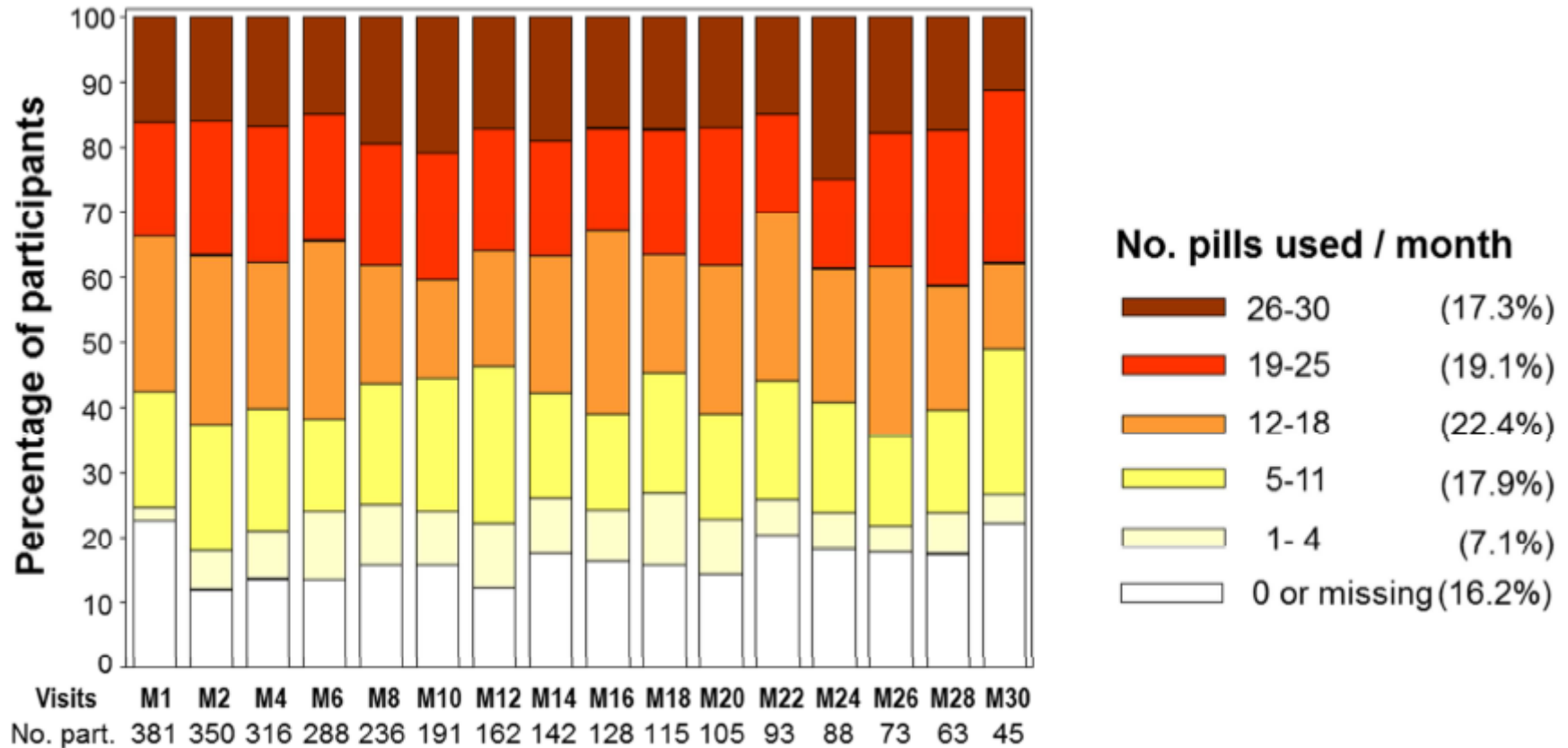
HIV acquisition is rare in MSM taking ≥ 4 doses of PrEP per week.

HIV incidence (cases per 100 person-years) by PrEP doses per week in iPrEx OLE



Grant RM, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis.* 2014;14(9):820-829.

PrEP dosing varied in IPERGAY.



Molina JM, et al. On demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med 2015;373:2237.

Case 3



- A 27 year-old gay man in generally good health presents to establish care.
- He has had a cold with fever, sore throat, and swollen glands for 2 days; taking frequent ibuprofen
- Unprotected anal sex with 1 primary and 2 occasional male sex partners; most recently 10 days ago
- HIV antibody and HBsAg negative; creatinine normal
- Interested in PrEP

Would you...

A. Start PrEP

B. Send an HIV viral load and base the PrEP decision on the result

C. Wait until his cold has improved and he's stopped ibuprofen; then start PrEP

D. Start PEP, then transition to PrEP after 28 days

Remember features of acute HIV

FEATURE	FREQUENCY (%)
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.



Case 3, follow-up

- HIV RNA 2.5 million; antibody seroconversion within one week
- **Acute HIV and PrEP:**
 - Patients may be symptomatic from acute HIV but have negative serologic testing (i.e., in the “window period”).
 - In clinical trials of PrEP, drug resistance has been seen in those who were in the window period at enrollment.
 - Use of the 4th-generation antibody/antigen test decreases but does not eliminate the window period.
 - Send an HIV RNA if in doubt.

Resistance is rare but occurs in those who are in the window period upon PrEP initiation.

TRIAL	RESISTANCE AMONG THOSE INFECTED AT ENROLLMENT	RESISTANCE AMONG THOSE INFECTED LATER IN THE STUDY
iPrex	1 of 8 in the placebo arm 2 of 2 in the PrEP arm	0 of 64 in the placebo arm 0 of 36 in the PrEP arm
Partners PrEP	0 of 6 in the placebo arm 2 of 8 in the PrEP arms	0 of 52 in the placebo arm 0 of 30 in the PrEP arms
TDF2	0 of 2 in the placebo arm 1 of 1 in the PrEP arm	1 of 24 in the placebo arm 0 of 9 in the PrEP arm
TOTAL	1 of 16 in placebo arms 5 of 11 in PrEP arms	1 of 140 in placebo arms 0 of 75 in PrEP arms

Of 7 subjects who had drug resistance, 5 were unknowingly infected with HIV when they started PrEP.

Case 4

- 48 year-old man referred for PrEP
- Obesity, hypertension, sleep apnea
- Monogamous with one male partner who is HIV infected but virologically suppressed
- HIV antibody/antigen and HBsAg negative; creatinine 1.09 (eGFR > 60)
- He asks if PrEP for him is worthwhile since his partner is undetectable.

Would you recommend PrEP?

A. Yes

B. No



The utility of PrEP on top of HIV treatment is unknown.

No

- HIV treatment prevents transmission; the additional benefit of PrEP may not outweigh its risks, however small.

Yes

- Viral rebound may occur because of poor ART adherence or other reasons.
- People may not be monogamous.
- CDC guidelines support PrEP in this context.



ART substantially reduces HIV transmission.

- **HPTN 052 study:** HIV treatment reduced HIV transmission by 96% in serodiscordant couples (incidence with ART 0.1 [0-0.4] per 100 person-years)⁽¹⁾
 - **IAS 2015:** 0 transmissions after the HIV-infected partner was stably suppressed on ART.
 - **Opposites Attract study:** 0 HIV transmissions in 152 serodiscordant MSM couples despite ~6,000 episodes of condomless anal sex (incidence 0 [0-4] per 100 couple-years)⁽²⁾

1. Cohen MS, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493-505.
2. Grulich AE, et al. HIV in male serodiscordant couples in Australia, Thailand, and Brazil. CROI, 2015. Abstract 1019LB.

A middle path: PrEP as a bridge to ART

- **Study:** Partners PrEP Demo Project
- **Population:** 1,013 heterosexual serodiscordant couples
- **Intervention:** PrEP until seropositive partner on ART for 6 months
- **Results:** 96% risk reduction compared to a historical control (incidence = 0.2 [0-1.3] per 100 person-years)

Baeten J, et al. Near elimination of HIV transmission in a demonstration project of PrEP and ART. CROI, 2015. Abstract 24.

Case 5

- 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.

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.

Case 6

- A 36 year-old woman and her 39 year-old husband present to discuss conception.
- He's HIV infected and virologically suppressed on ART; she's HIV-negative.
- They want to conceive a child and cannot afford sperm washing.
- They ask if you would recommend PrEP for her and condomless sex in this situation.

What would you say?

A. Yes

B. No

PrEP may be part of a conception strategy but may be unnecessary.



- No increased birth defects with tenofovir-emtricitabine among women in the Antiretroviral Pregnancy Registry ⁽¹⁾
- Other reproductive strategies for such couples may be limited to non-existent.
- However, modeling suggests PrEP adds little, assuming ART and other factors are optimized ⁽²⁾

1. Antiretroviral pregnancy registry interim report. 2014. Available from: www.apregistry.com/forms/exec-summary.pdf.

2. Hoffman RM, et al. Benefits of PrEP as an adjunctive method of HIV prevention during attempted conception between HIV-uninfected women and HIV-infected male partners. *J Infect Dis.* 2015;212(10):1534.

PrEP uncertainties and questions

- Efficacy of “on-demand” PrEP for infrequent sex
- Benefit of PrEP in the context of HIV treatment
- Utility of PrEP in the peri-conception period

Take-home points

- Daily tenofovir-emtricitabine substantially reduces the risk of HIV infection in individuals at high risk.
- Serious side effects are rare; renal function must be monitored periodically while on PrEP.
- Before starting PrEP, test for acute HIV if there are any suggestive clinical signs or symptoms.
- There is no evidence of adverse pregnancy outcomes among women who conceive on tenofovir-emtricitabine.

Thank you!

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