NATIONAL LGBT HEALTH EDUCATION CENTER

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What's new in PrEP and STIs? Cases from a sexual health clinic

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Our Roots

Fenway Health

- Independent 501(c)(3) FQHC
- Founded 1971
- Integrated Primary Care Model, including Behavioral Health, HIV/STI prevention and care
- 35,000 patients
  - Half LGBT
  - 10% transgender

The Fenway Institute

- Research, Education and Training, Policy

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Today's Faculty

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Disclosure

I have no financial conflicts of interest.

Learning objectives

Manage cases that highlight:

- Developments in PrEP

- HIV prevention for transgender people

- Emerging STIs and STI prevention

The cases presented here are adaptations of real clinical cases, with identifying information removed.

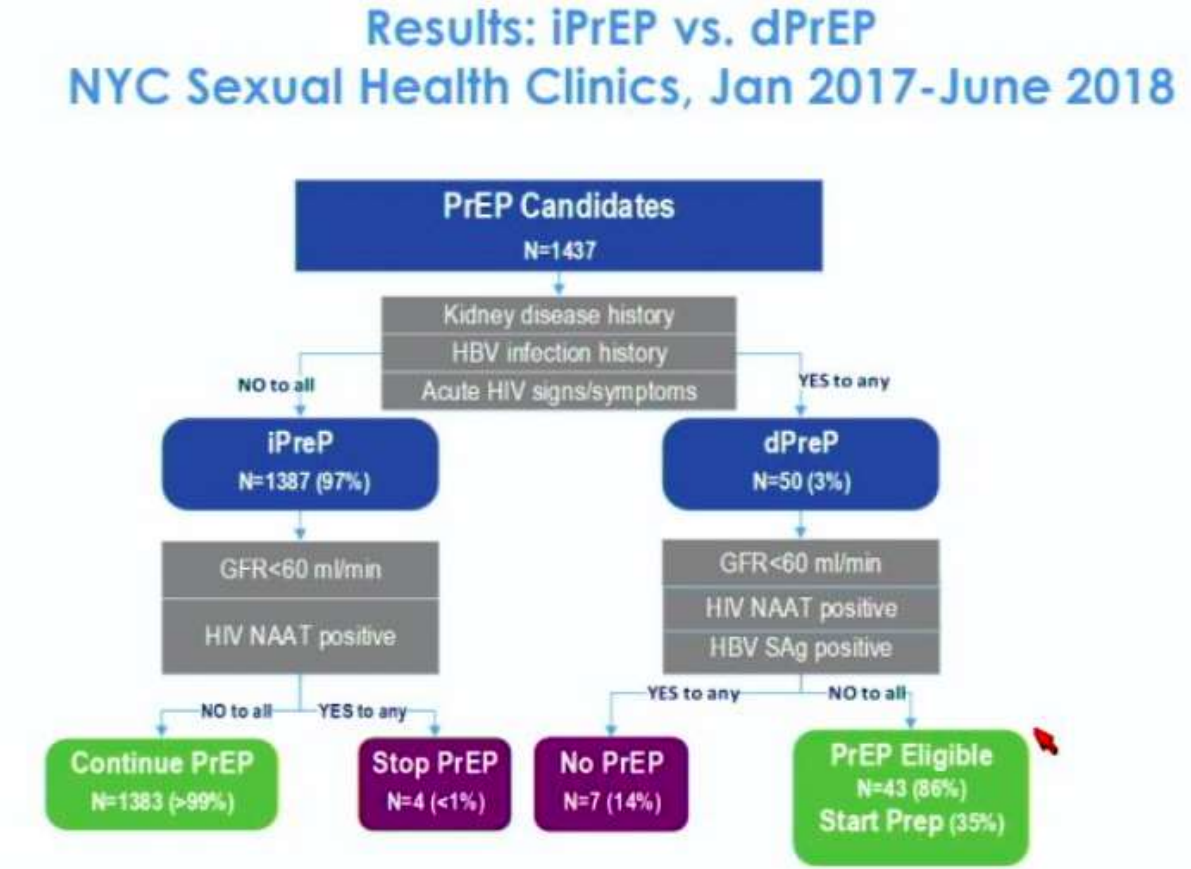
The cases focus on populations at greatest epidemiologic risk for HIV and STIs (gay, bisexual, and other MSM; transgender people). These populations are not representative of all LGBTQ people.

Case 1

- A 23-year-old man presents at a drop-in center for STI screening.
- He is sexually active with more than 100 male partners per year, rarely using condoms. He describes himself as an escort.
- He uses crystal methamphetamine by injection daily.
- He has no chronic medical problems and takes no medications.
- His last HIV/STI screen one year ago.
- He last had sex 2 weeks ago.

How quickly can he start PrEP, assuming he does not have HIV?

Same-day access may increase PrEP uptake.



Mikati, CROI 2019, Abstract #962

Other strategies to foster PrEP uptake

Provide PrEP in non-traditional venues

- Pharmacies, mobile vans, community organizations

Rapidly assess for medical contraindications

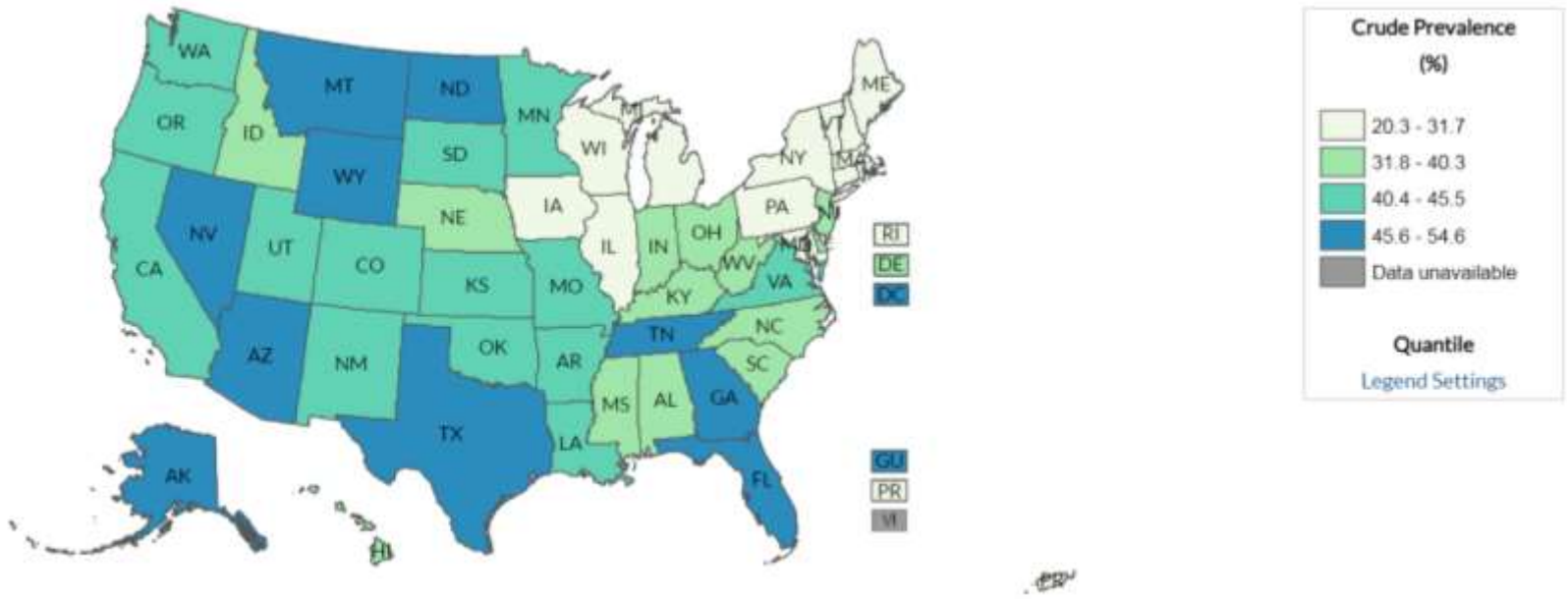
- Point of care creatinine testing

Navigate benefits enrollment

- Immediate access to a PrEP navigator, state/local assistance programs

How many PrEP candidates are engaged in primary care?

CDC's BRFSS: "Do you have one person you think of as your personal doctor or health care provider?"



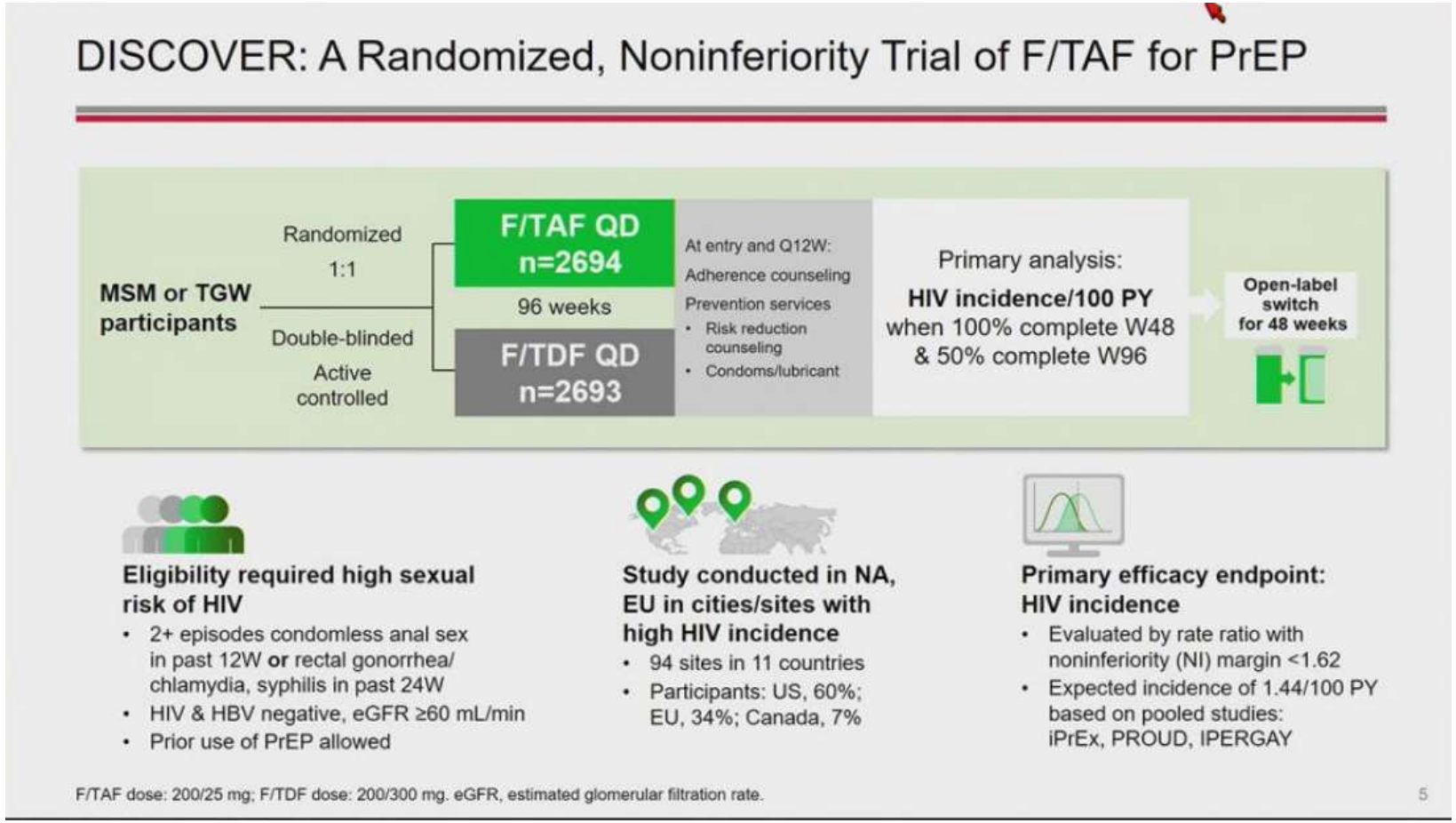
Behavioral Risk Factor Surveillance System, 2017

Case 2

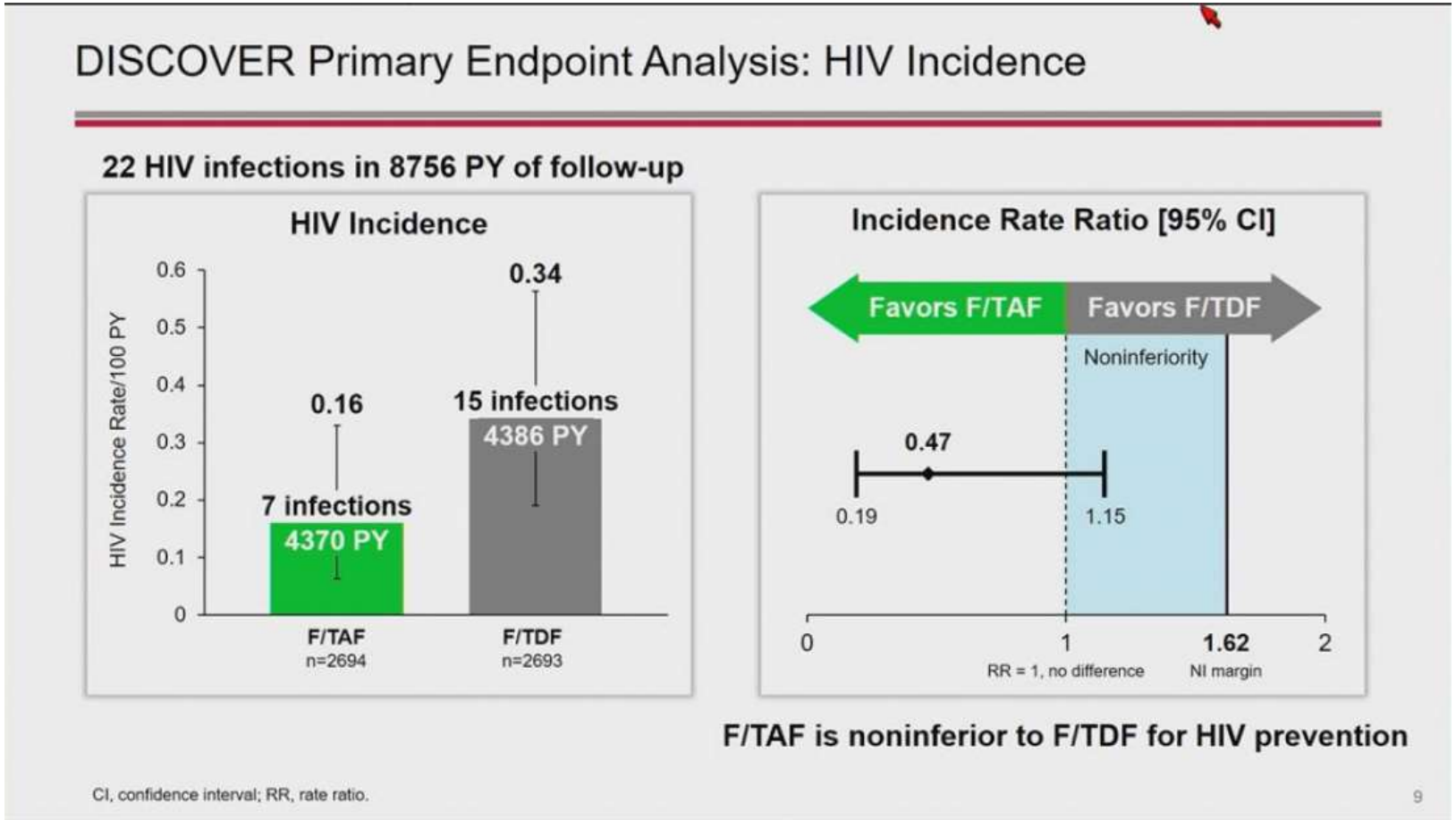
- A 38-year-old man presents seeking PrEP.
- His partner was diagnosed with HIV 3 weeks ago and is not yet suppressed on ART. They have been having condomless anal sex.
- The patient has a history of severe hypertension, heart failure, and chronic kidney disease (eGFR ~50).
- He takes carvedilol, lisinopril, furosemide.

What are his options for PrEP, assuming he does not have HIV?

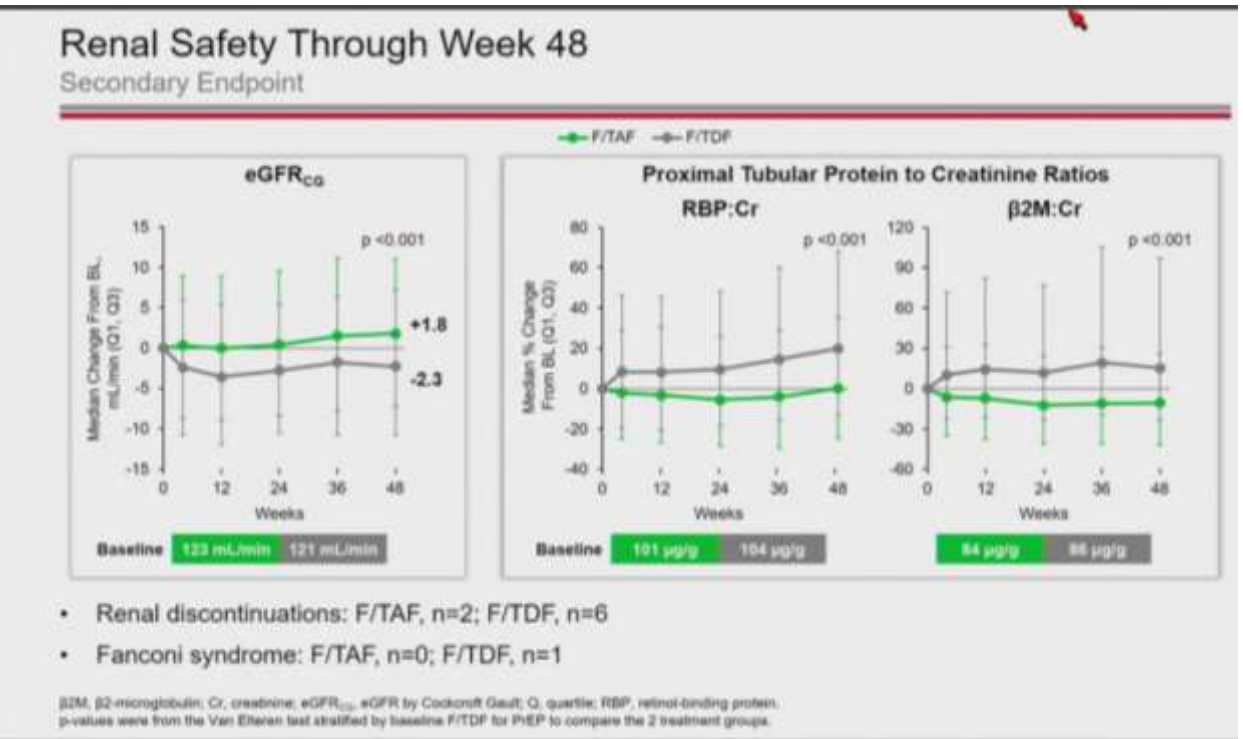
TAF-FTC is non-inferior to TDF-FTC for PrEP.

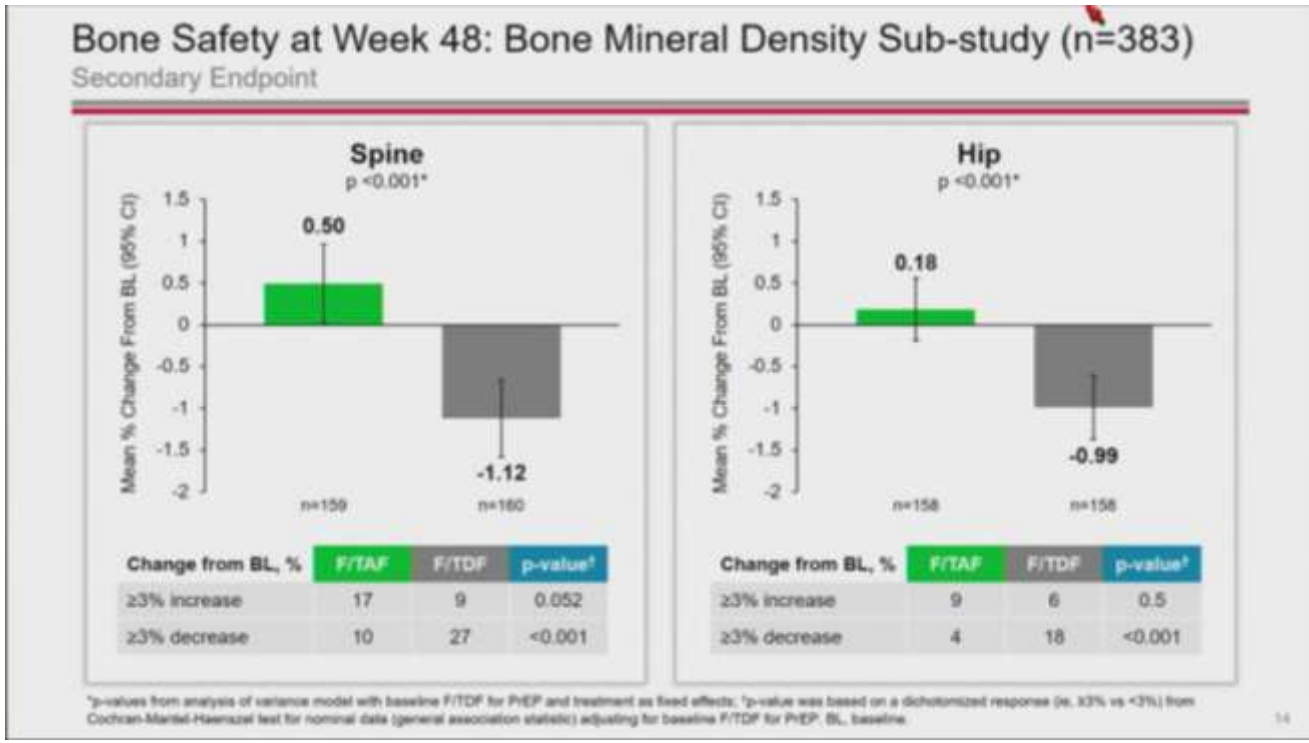


TAF-FTC is non-inferior to TDF-FTC for PrEP.



Renal and bone safety favor TAF.





Questions about TAF-FTC for PrEP

- Will the favorable renal and bone safety markers be worth the presumably increased cost for the average PrEP user?
- Could the renal and bone advantages of TAF-FTC be overcome by using TDF-FTC in an on-demand fashion?
- Will there be assistance programs for PrEP with TAF-FTC?
- Does TAF-FTC work in cisgender and transgender women?

Case 3

- A 29-year-old non-binary person assigned male sex at birth presents because of persistent dysuria.
- They are sexually active with cisgender and transgender male and female partners, having oral, penile-vaginal, and anal sex.
- They first came to care 3 weeks ago with dysuria and scant urethral discharge. A urinary sediment showed 15-20 WBC. They received empiric ceftriaxone/azithromycin. A urine gonorrhea/chlamydia NAAT ultimately returned negative.
- One week ago, they returned with the same symptoms. A urinary sediment showed 15-20 WBC. They were given metronidazole and 7 days of doxycycline. There has been no improvement.

What is the best next step in management?

Mycoplasma genitalium: An emerging sexually-transmitted pathogen

- First identified in men with non-gonococcal urethritis (NGU) in 1980
- Major cause of NGU; more common than gonorrhea but less common than chlamydia
- Diagnosed by nucleic acid detection; culture challenging
- Treatment can be difficult:
  - Intrinsically resistant to beta-lactams
  - Doxycycline ineffective
  - Azithromycin increasingly ineffective
  - Moxifloxacin usually effective

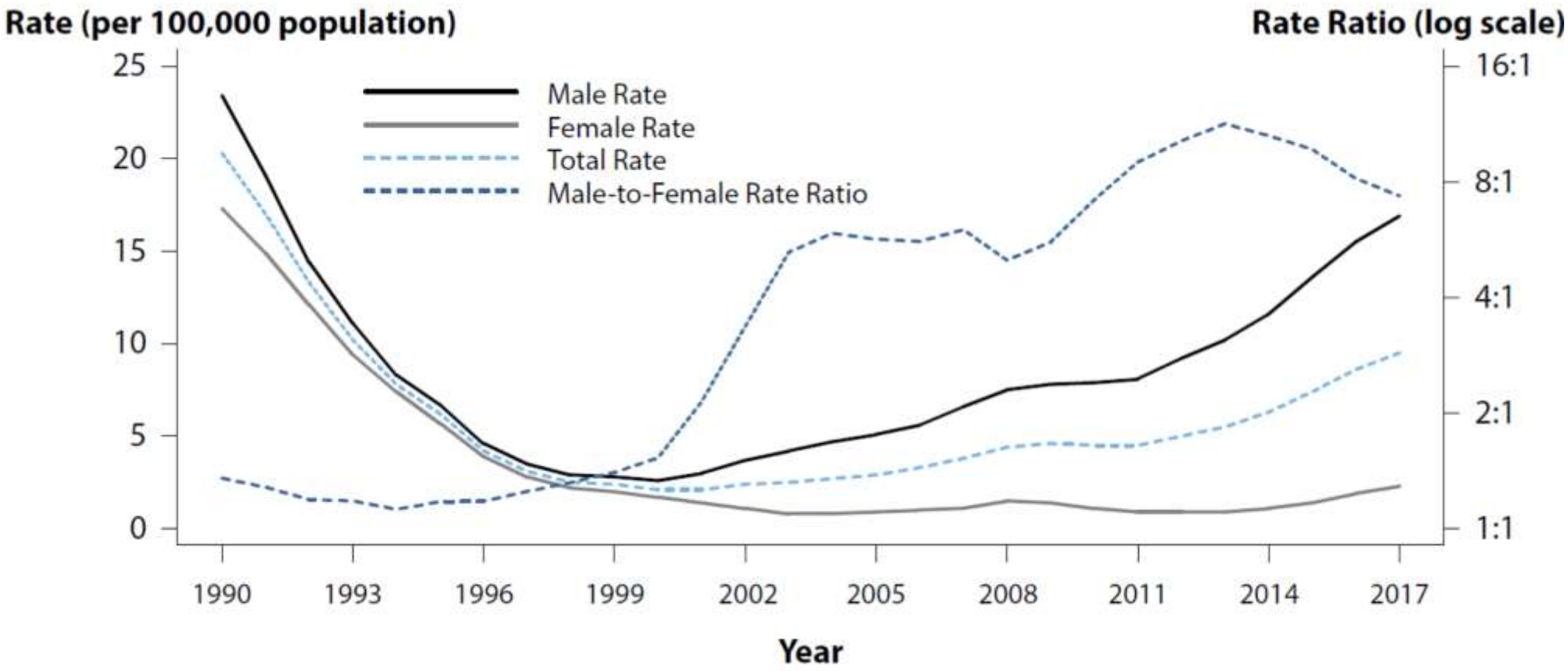
Horner PJ, Martin DH. Mycoplasma genitalium infection in men. J Infect Dis. 2017;216(Suppl 2):S396-S405.
Workowski KA, Bolan G. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(3).

Case 4

- A 32-year-old man presents to the emergency room with blurry vision and floaters in his left eye for 3 days.
- He has sex with multiple male partners, rarely uses condoms, on TDF-FTC for PrEP for 1 year with excellent adherence
- His examination shows: Left eye vitritis and chorioretinitis
- His laboratory studies show: Treponemal antibody positive, RPR 1:258
- He receives 2 weeks of intravenous penicillin with partial recovery of vision.

He is unsure he can increase condom usage. What can he do to avoid syphilis re-infection?

Rates of reported syphilis are increasing.



Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2017*. Atlanta: U.S. Department of Health and Human Services; 2018.

Ocular syphilis is on the rise.

Morbidity and Mortality Weekly Report

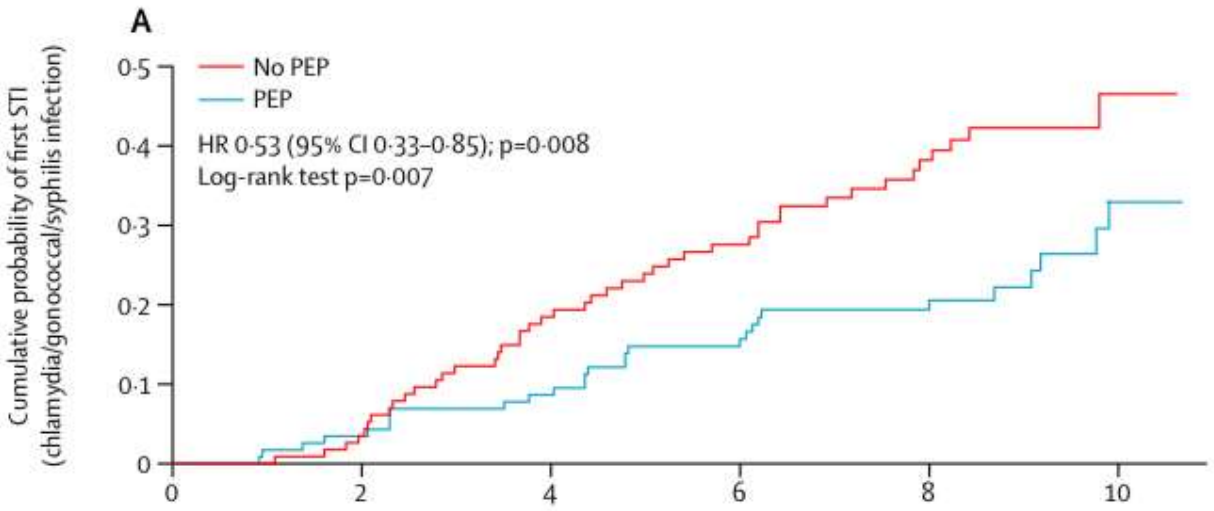
Ocular Syphilis — Eight Jurisdictions, United States, 2014–2015

Sara E. Oliver, MD[1,2]; Mark Aubin[3]; Leah Atwell, MPH[4]; James Matthias, MPH[4,5]; Anna Cope, PhD[5,6]; Victoria Mobley, MD[6]; Alexandra Goode, MSc[7]; Sydney Minnerly, MA[8]; Juliet Stoltey, MD[9]; Heidi M. Bauer, MD[9]; Robin R. Hennessy, MPH[5,10]; Dawne DiOrio, MPA[5,11]; Robyn Neblett Fanfair, MD[12]; Thomas A. Peterman, MD[5]; Lauri Markowitz, MD[2]

Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2017*. Atlanta: U.S. Department of Health and Human Services; 2018.

Doxycycline PEP prevents syphilis and chlamydia among MSM.

- 232 MSM in a trial of open-label, on-demand PrEP with TDF-FTC
- Randomized to doxycycline within 24 hours of sex or no PEP
- Doxycycline reduced chlamydia and syphilis infections but not gonorrhea



Molina JM, Lancet Infect Dis, 2018

PEP with doxycycline is generally well-tolerated.

	PEP (n=116)	No PEP (n=116)	p value
Any adverse events	106 (91%)	104 (90%)	0·65
Any serious adverse events	5 (4%)	10 (9%)	0·18
Any grade 3 or 4 events	4 (3%)	8 (9%)	0·24
Treatment discontinuation because of adverse events	8 (7%)	NA	..
Gastrointestinal adverse events	62 (53%)	47 (41%)	0·05
Drug-related gastrointestinal adverse events	29 (25%)	16 (14%)	0·03
Nausea or vomiting	10 (9%)	3 (3%)	..
Abdominal pain	14 (12%)	5 (4%)	..
Diarrhoea	6 (5%)	9 (8%)	..
Other gastrointestinal disorders	5 (4%)	1 (1%)	..

Other known issues:

- Sun sensitivity
- Pill esophagitis
- Reduced absorption when administered concurrently with di- and trivalent cations (e.g., calcium)

Molina JM, Lancet Infect Dis, 2018

My approach in this case

- Counseled about what is known and not known about doxycycline PEP
- Discussed doxycycline adverse effects, known and presumed (antimicrobial resistance)
- Reviewed that this use of doxycycline is off-label
- The patient opted to take doxycycline PEP and is doing well with this strategy after one year.

Case 5

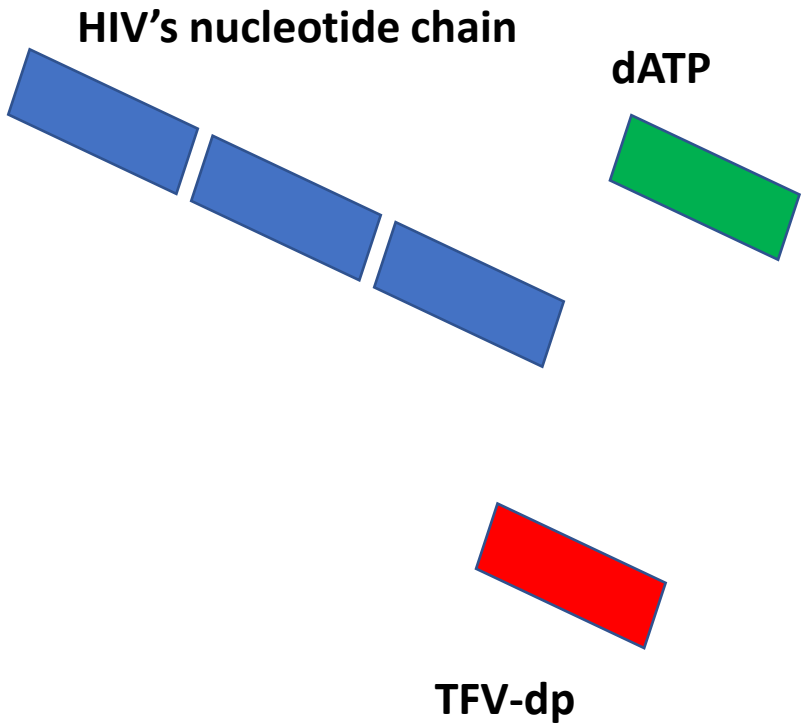
- A 26-year-old trans woman whose identity has shifted from that of a gay man to a genderfluid person to a trans woman over the past 1.5 years presents in follow-up.
- She is starting estrogen and spironolactone for gender affirmation.
- She has a history of syphilis and rectal gonorrhea/chlamydia.
- She has multiple cisgender male partners and takes TDF-FTC with fair adherence.

Patient's question: Will estrogen impact the effectiveness of PrEP?

Concerns about rectal drug levels in TGW taking PrEP and estradiol

Background:

- Tenofovir and other NRTIs work by halting production of HIV's genetic material (string of nucleotides)
- In the body, tenofovir becomes tenofovir diphosphate (TFV-dp).
- TFV-dp competes with the body's naturally occurring deoxynucleotides (dATP).
- dATP's and TFV-dp's activities are inversely correlated.
- Female hormones can affect nucleotide balance.



Cottrell ML, Clin Infect Dis, 2019

Concerns about rectal drug levels in TGW taking PrEP and estradiol

Population:

- 4 TGW and 8 cisgender control subjects (cisgender men and post-menopausal women)
- All taking TDF-FTC for HIV treatment or PrEP

Study procedures: Blood and rectal tissue obtained for hormone and drug level monitoring

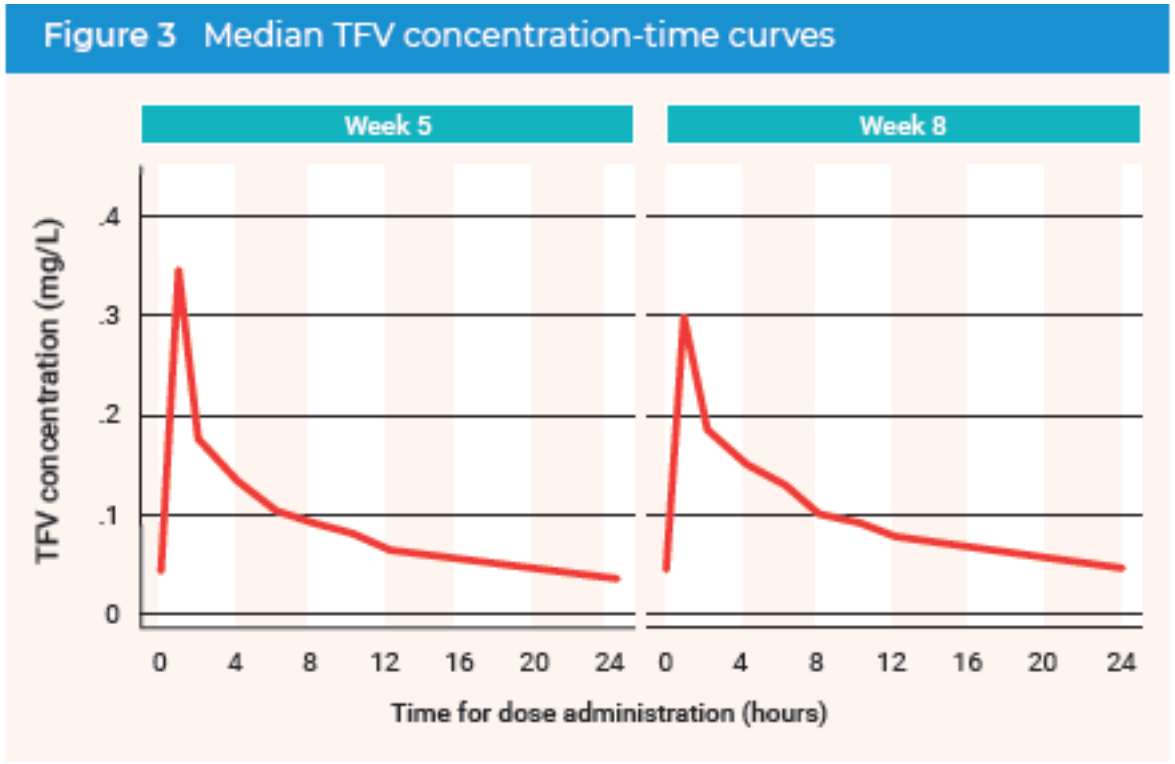
Results:

- Blood and rectal tissue tenofovir/FTC, metabolite, and deoxynucleotide concentrations not different across groups
- Median TFVdp:dATP ratio 7-fold lower in transgender versus cisgender participants, inversely correlated with estradiol and progesterone

Cottrell ML, Clin Infect Dis, 2019

Drug-drug interactions?: the iFACT study

- **Population:** 20 transgender women who had not undergone orchiectomy
- **Methods:**
  - Prescribed estradiol valerate and cyproterone acetate weeks 0-5 and 8-15
  - Prescribed PrEP beginning week 3
- **Outcomes:**
  - No effect of PrEP on estradiol or testosterone levels
  - Tenofovir levels 13% lower with hormones, likely not clinically significant



Hiransuthikul A, et al. Drug-drug interactions between the use of feminizing hormone therapy and pre-exposure prophylaxis among transgender women: the iFACT study. International AIDS Conference. Amsterdam, 2018. Abstract TUPDX0107LB.

Does PrEP work in transgender women?

- Only one RCT – iPrEX – enrolled a significant number of transgender women.
  - 2499 participants
  - 339 (14%) classified as transgender women
- In a post-hoc, intention-to-treat analysis, the HR for HIV in the PrEP group was 1.1 [95% CI 0.5-2.7], **BUT**
  - None of the transgender women who acquired HIV had detectable drug at the time of seroconversion.
  - No transgender woman seroconverted who had drug levels indicative of 4 or more doses of PrEP per week.

Deutsch MB, Glidden DV, Sevelius J, et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEX trial. Lancet HIV. 2015;2(12):e512.

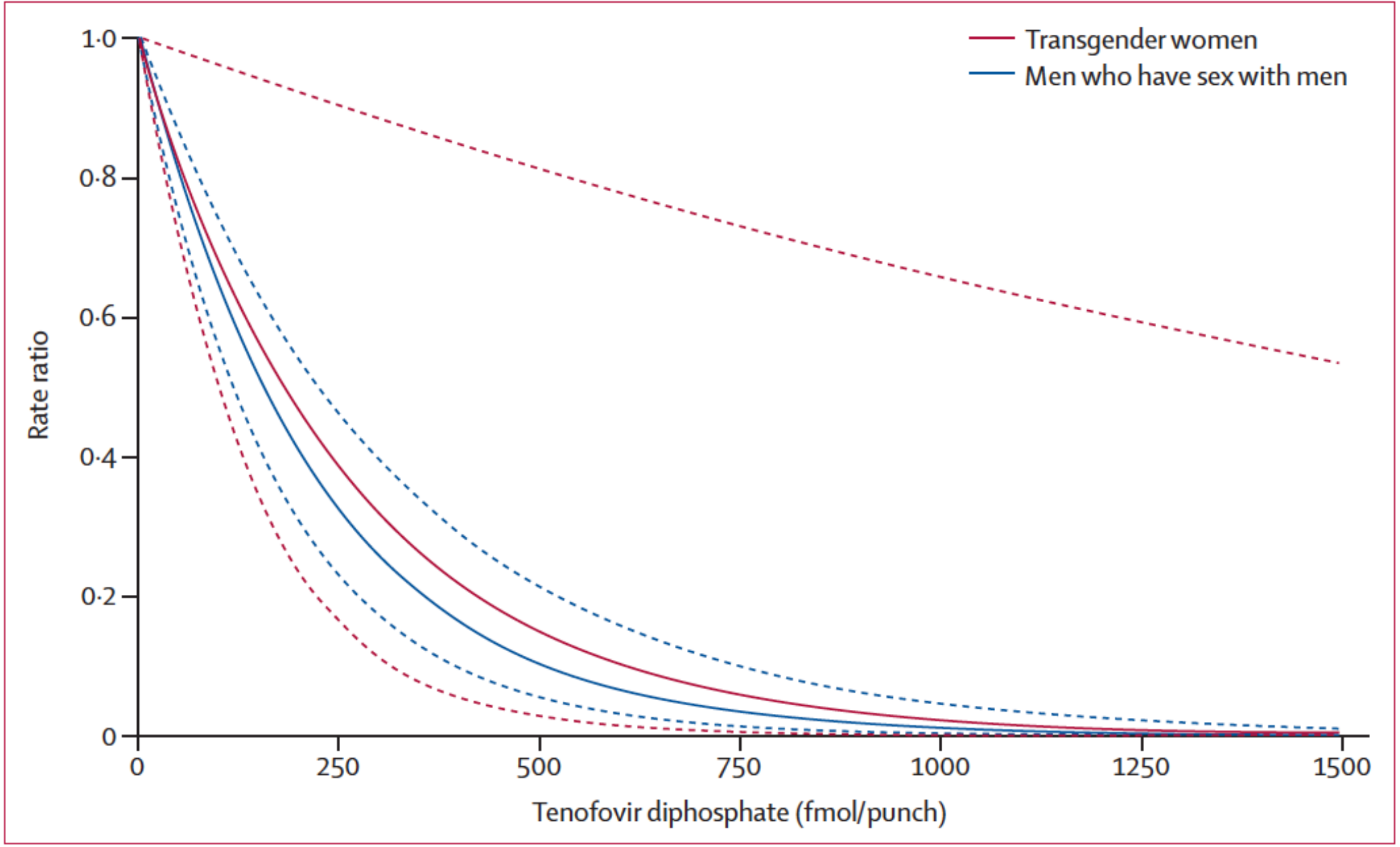


***Figure 3*: Rate ratios for HIV infection in the iPrEx open-label extension by gender**

Deutsch MB, Glidden DV, Sevelius J, et al. HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEX trial. Lancet HIV. 2015;2(12):e512.

CDC Clinical Practice Guidelines for PrEP

"…PrEP has been shown to reduce the risk for HIV acquisition during anal sex and penile-vaginal sex. Therefore, its use may be considered in all persons at risk of acquiring HIV sexually."

Preexposure prophylaxis for the prevention of HIV infection in the United States – 2017 update. US Public Health Service. 2018.

Case 6

- A 45-year-old bisexual man presents for STI screening.
- He is sexually active with one female partner in the US, but when he travels to Europe for work (10 times per year), has sex with men and women he meets online. He does not use condoms for sex.
- He wants to take PrEP but feels daily dosing is excessive

Would you recommend on-demand TDF-FTC for him?

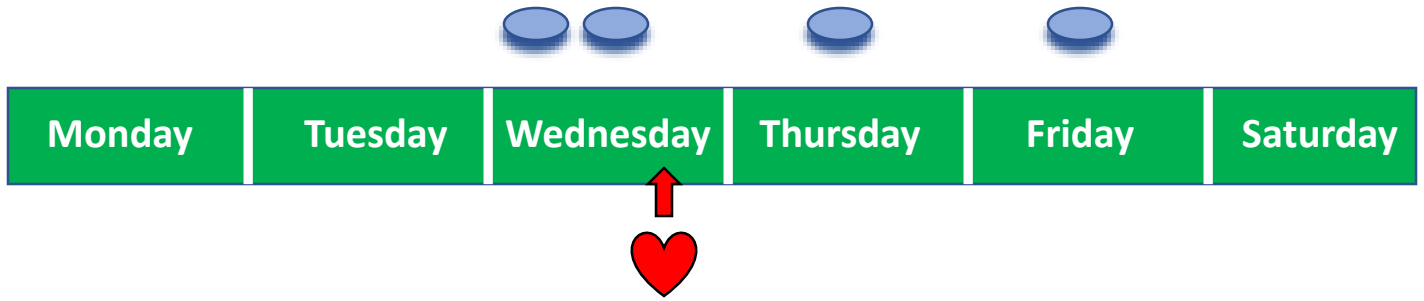
Consider on-demand PrEP

Pericoital TDF/emtricitabine PrEP, also known as on-demand, event-driven, or "2-1-1" dosing may be considered as an alternative to daily PrEP for MSM with infrequent sexual exposures (evidence rating AIa). This regimen is not recommended in other risk groups or in patients with active HBV infection because of the risk of hepatitis flare and hepatic decompensation (evidence rating BIIa).

Saag M, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults. JAMA. 2018;320(4):379-396.

IPERGAY 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
- **2-1-1 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.

My approach in this case

- Counseled about what is known and not known about on-demand PrEP
- Discussed concerns that rare use may not be protective
- Reviewed that this use of TDF-FTC is off-label
- The patient elected to try on-demand TDF-FTC.

Summary

- Initiate PrEP in a same-day fashion for people at high risk of HIV
- Consider TAF-FTC for PrEP candidates with renal or bone disease
- Treat/test for *Mycoplasma genitalium* in the setting of persistent/recurrent urethritis
- Consider doxycycline PEP for MSM with a high risk of syphilis
- Prescribe PrEP for transgender women with a high risk for HIV
- Consider on-demand PrEP for MSM

Questions?

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