

HIV Pre Exposure Prophylaxis

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Evidence-Based HIV Prevention Strategies

- **Risk Reduction**
 - Condom access and distribution
 - Health education and risk reduction counseling
 - Needle and syringe exchange
 - STI screening, testing and treatment
- **HIV testing and treatment**
- **Post-exposure prophylaxis (PEP)**
- **Pre-exposure prophylaxis (PrEP)**

Multiple, proven prevention strategies



What Is HIV PrEP?

Is when HIV negative people at very high risk for acquiring HIV take tenofovir/emtricitabine daily to:

- Lower their chances of getting infected when exposed **sexually** or through **injection drug use** to someone who is HIV positive.

Taken daily PrEP can lower the risk of getting HIV from

- Sex by more than 90%
- Injection drug use by more than 70%

PrEP is highly effective for preventing HIV if it is used as prescribed.

PrEP is not a substitution for other HIV prevention interventions such

PrEP does not protect against other STIs

Available Medications and regimens for HIV PrEP

Daily oral **FTC/TDF** recommended for all adults and adolescents at risk for HIV through **sex or IDU**

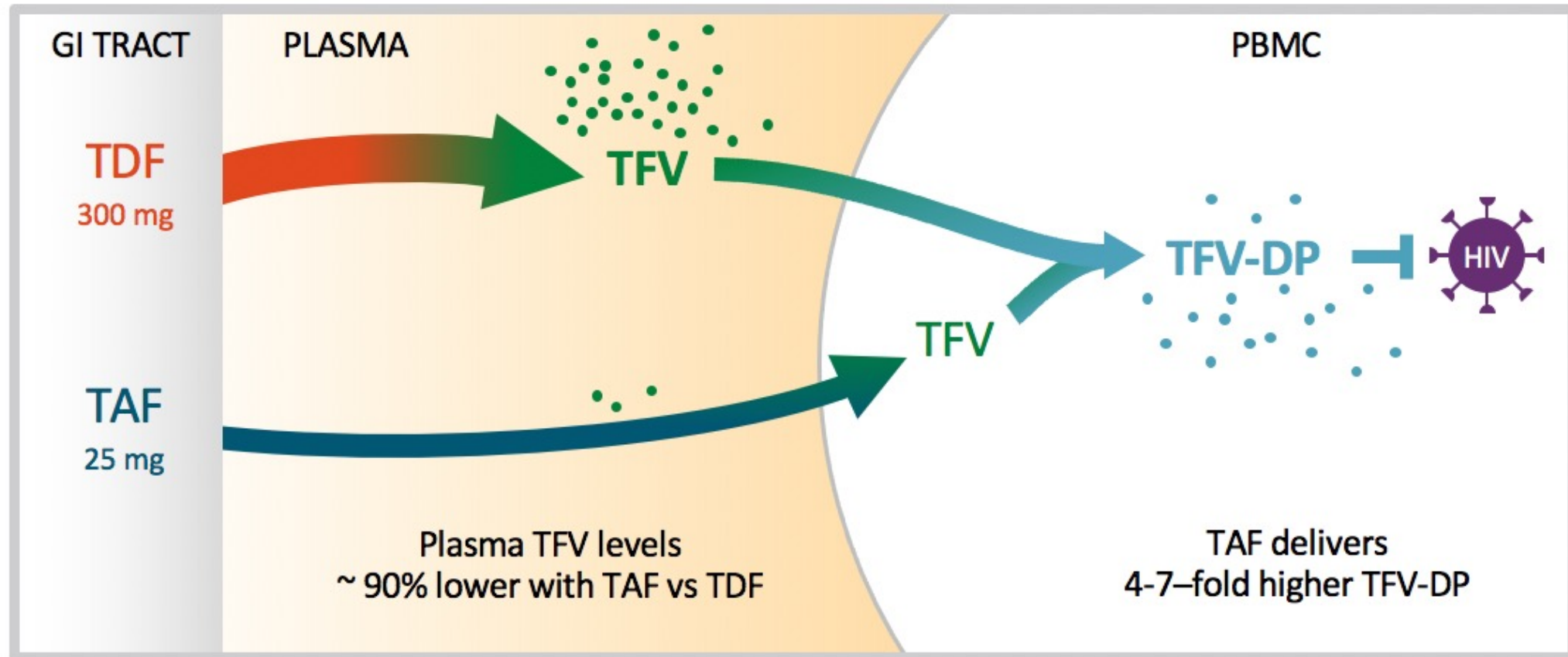
- **FDA approved**
- On-demand use of FTC/TDF (2:1:1) for MSM only. **Off-label per FDA but an option in IAS-USA, WHO and Canadian guidelines**

Daily oral **FTC/TAF** recommended for adults and adolescents at risk for HIV through **sex, excluding people at risk through receptive vaginal sex.**

- **FDA approved only MSM or Transgender women**
- On-demand use not recommended



Higher TFV-DP Levels in PBMCs With TAF vs TDF



Ruane. JAIDS. 2013;63:449. Sax. JAIDS. 2014;67:52. Sax. Lancet. 2015;385:2606.

Slide credit: clinicaloptions.com

TAF is a pro-drug that can be absorbed quicker than TDF and can be prescribed in smaller doses, as higher levels of the active drug, tenofovir diphosphate, is seen in the cells

Indications for PrEP:

For adults or adolescents weighing >35 kg *without* acute or established HIV infection ONLY

MSM	Heterosexual Men/Women	People Who Inject Drugs
<ul style="list-style-type: none"> ▪ Any male sex partner in past 6 months ▪ Not in monogamous relationship with a recently tested, HIV-negative man <p style="text-align: center;"><i>And ≥1 of These Criteria</i></p> <ul style="list-style-type: none"> ▪ Any anal sex without a condom in past 6 months ▪ Bacterial STI (syphilis, gonorrhea, or chlamydia) in past 6 months 	<ul style="list-style-type: none"> ▪ Any sex with opposite sex partner in past 6 months ▪ Not in monogamous relationship with a recently tested, HIV-negative partner <p style="text-align: center;"><i>And ≥1 of These Criteria</i></p> <ul style="list-style-type: none"> ▪ Infrequent condom use with ≥1 partner(s) with unknown HIV status at substantial risk of HIV infection (PWID or MSM) ▪ Is in ongoing relationship with HIV-positive partner with unsuppressed HIV-1 RNA ▪ Bacterial STI (syphilis, gonorrhea in females/males) in last 6 months 	<ul style="list-style-type: none"> ▪ Any injection of drugs not prescribed by a clinician in past 6 months <p style="text-align: center;"><i>And ≥1 of These Criteria</i></p> <ul style="list-style-type: none"> ▪ Any sharing of injection/drug preparation equipment in past 6 months ▪ Risk of sexual acquisition

Contraindications to TDF/FTC for PrEP

Active HIV Infection

Need HAART: 3-active medications

Renal Dysfunction

TDF: Do not start if CrCl <60 mL/min
Stop if CrCl <50 mL/min

TAF: If CrCl < 30 mL/min

Allergy to TDF or FTC

Currently no alternative

Caution with active HBV Infection as discontinuation of TDF/FTC can lead to hepatitis flair

FTC/TDF: emtricitabine/tenofovir disoproxil fumarate;

TAF: tenofovir alafenamide

<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>

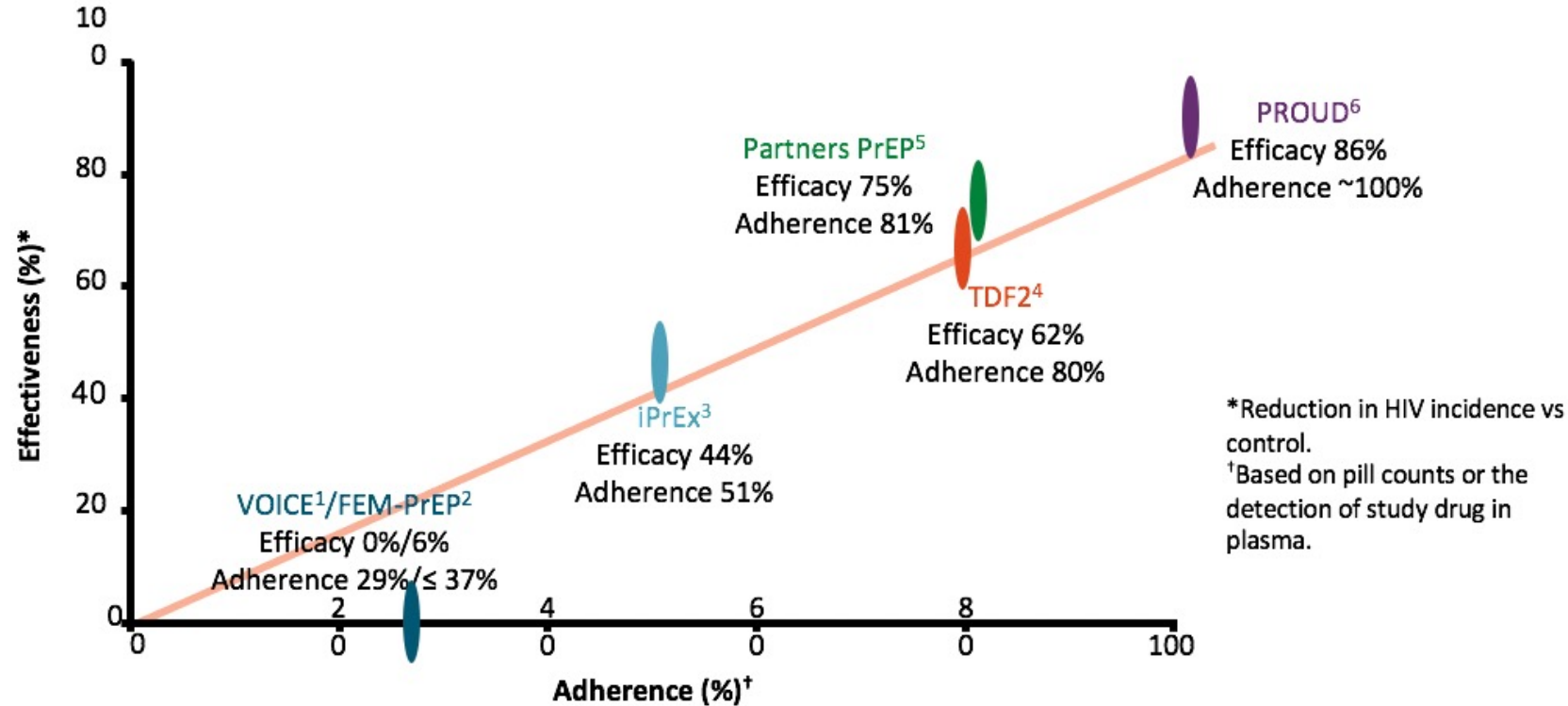
Once Daily Oral TDF-Based PrEP Efficacy in Clinical Trials

Population	Study	Study Drug	Control	Efficacy for Reducing HIV Incidence, %
MSM	iPrEx ¹	FTC/TDF (n = 1251)	Placebo (n = 1248)	44.0 (<i>P</i> = .005)
HS men & women	Partners PrEP ²	FTC/TDF (n = 1583)	Placebo (n = 1586)	75.0 (<i>P</i> < .001)
	TDF ³	FTC/TDF (n = 611)	Placebo (n = 608)	62.2 (<i>P</i> = .03)
PWID	BTS ⁴	TDF (n = 1204)	Placebo (n = 1207)	48.9 (<i>P</i> = .01) If detectable TDF: 73.5 (<i>P</i> = .03)



Slide credit: clinicaloptions.com

Select Daily Oral FTC/TDF PrEP Trials: Effectiveness Improves With Adherence



1. Marrazzo. NEJM. 2015;372:509. 2. Van Damme. NEJM. 2012;367:411. 3. Grant. NEJM. 2010;363:2587.
4. Thigpen. NEJM. 2012;367:423. 5. Baeten. NEJM. 2012;367:399. 6. McCormack. Lancet. 2016;387:53.



Slide credit: clinicaloptions.com

On-Demand Oral FTC/TDF PrEP in MSM

NOT FDA APPROVED

On-demand regimen for each sexual intercourse: **2:1:1**

- FTC/TDF tablets 2-24 hr before sex; 1 FTC/TDF tablet 24 hr after the first drug intake, and 1 FTC/ TDF tablet 24 hr later

In case of multiple subsequent sexual intercourses

- FTC/TDF tablet per day until the last sexual intercourse, then 1 FTC/TDF tablet per day for 2 further days

On-demand FTC/TDF should not be used for³

- Heterosexual men and women,
- Transgender men and women,
- Those with HBV infection

Study	N	Median Pills/Mo	Risk Reduction, %	P Value
Placebo controlled, randomized ¹	400	15	86	.002

Double-blind, randomized study of on-demand FTC/TDF vs placebo as PrEP for Men and TG women who have sex with men, with unprotected anal sex with ≥ 2 partners in ≤ 6 months¹

Summary of PrEP Eligibility by Regimen

Risk Group	Daily FTC/TDF	On-Demand (2:1:1) FTC/TDF	Daily FTC/TAF
MSM	Approved, guideline recommended	Off-label, guideline recommended	Approved, guideline updates pending
TG women	Approved, guideline recommended	Off-label, not recommended	Approved, guideline updates pending
Heterosexual women	Approved, guideline recommended	Off-label, not recommended	Off-label, not recommended, studies underway
Heterosexual men	Approved, guideline recommended	Off-label, not recommended	Approved, guideline updates pending
TG men	Approved, guideline recommended	Off-label, not recommended	Off-label, not recommended (unless risk from anal sex only)
PWID	Approved, guideline recommended	Off-label, not recommended	Off-label, not recommended



Slide credit: clinicaloptions.com

Engaging Patients and Initial Workup

If you are a talker

- Get to know your patient and her/his risk(s)
- Ask many questions
- Educate about signs and symptoms of STI's
- Don't forget about drug and alcohol use around sex
- Don't forget about shared paraphernalia

If you are a listener, get a brochure in your waiting area

Initial Workup

Determine clinical eligibility



Viral hepatitis

- HBsAg
- HBsAb
- HCV Ab



Renal function

- Creatinine
- eCrCl



HIV status

- Ag/Ab (4th gen)
- Rapid (blood)
- ELISA / EIA

CAUTION if active HBV!

eCrCl must be ≥ 60 mL/min

Must be HIV(-)
→ Maybe RNA, too?

US Public Health Service. PrEP Guideline – 2014.

SCREEN for STIs !!!

Initial Workup

Documented HIV-negative test (antigen/antibody test preferred) within 1 wk of initiating PrEP

No signs/symptoms of acute HIV infection in preceding month or on day of evaluation

Renal function requirements

- FTC/TDF: CrCl >60 mL/min
- FTC/TAF: CrCl >30 mL/min (or CrCl <15 mL/min if receiving chronic hemodialysis)

Screen for STIs; offer HAV and HPV vaccination

Documented HBV infection and vaccination status: vaccinate if susceptible

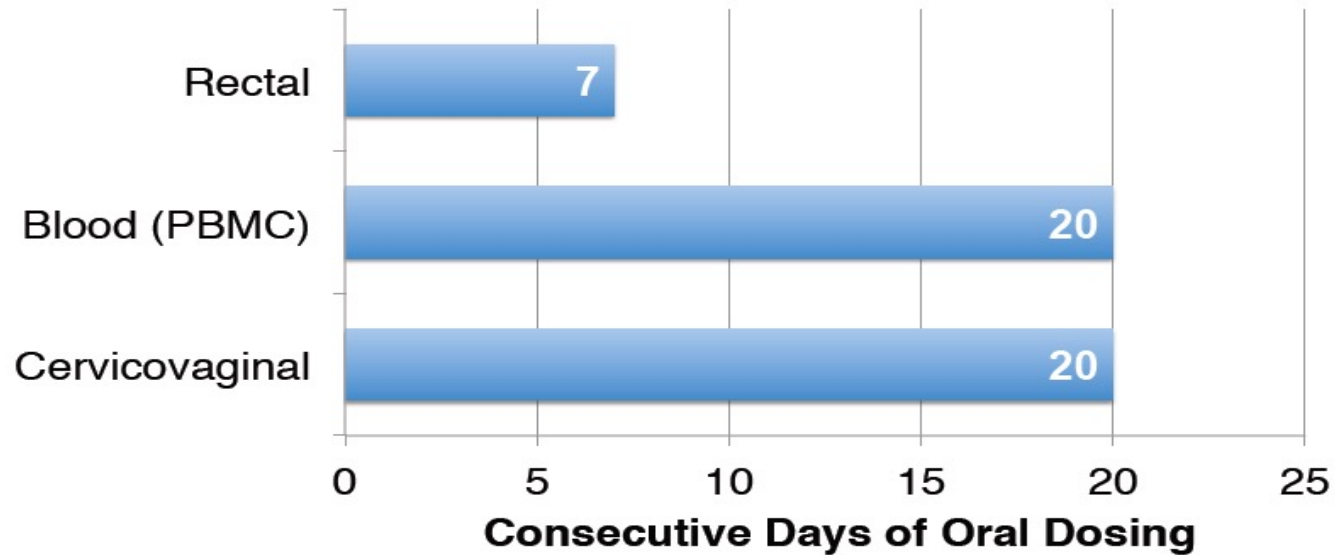
PrEP Monitoring Summary

Assessment	Initiation	At Least Every 3 Mos	At Least Every 6 Mos	At Least Every 12 Mos
HIV test: signs/symptoms of acute HIV	X	X		
Pregnancy test	X	X		
STI assessment	X	X		
STI testing	X		X	
Hepatitis B serology	X			
Renal function	X		X	
Assess HIV risk and PrEP indication*	X			X
Counsel on adherence and behavioral risk reduction	X	X		

*Based on provider discretion, can be done more frequently.

How long before I'm protected?

Time to Maximum Intracellular Concentration of Tenofovir Diphosphate (TFV-DP)



US Public Health Service. PrEP Guideline – 2014.

PrEP in Special Clinical Situations

■ Adolescents

- Limited information on potential for long-term toxicity (bone, renal)
- Adherence is a major challenge
- Disclosure issues
- **But young individuals have the most to gain from not acquiring HIV**

■ Pregnancy

- Limited data on PrEP safety and efficacy during pregnancy or breastfeeding³
- FTC/TDF widely used in HIV-positive persons, including pregnant women^{4,5}
- Providers should discuss the potential risks and benefits of PrEP use in pregnancy to enable the woman to make an informed decision³

■ Transgender (TG) individuals

- TG women 49 times more likely to be living with HIV than other reproductive-age adults¹ AND PrEP is effective and safe
- Complete sexual history should be taken before the initiation of PrEP, including type of sex, gender-affirming hormones, gender-affirming surgeries
- Testosterone can elevate serum creatinine and in TG women with intact testicles receiving PrEP plus feminizing hormones had 12% lower TFV plasma concentrations vs PrEP use without hormones⁴
- PrEP coadministration did not affect feminizing hormone levels

Conclusions

Primary care providers play a key role in delivering PrEP

PrEP is a safe and effective HIV prevention option

Daily oral FTC/TDF is the only FDA-approved PrEP medication for individuals at risk of HIV from receptive vaginal sex or IDU

- MSM ONLY have the option of on-demand (2:1:1) oral FTC/TDF dosing or daily oral FTC/TAF