Updates in HIV Prevention

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Our Roots

Fenway Health

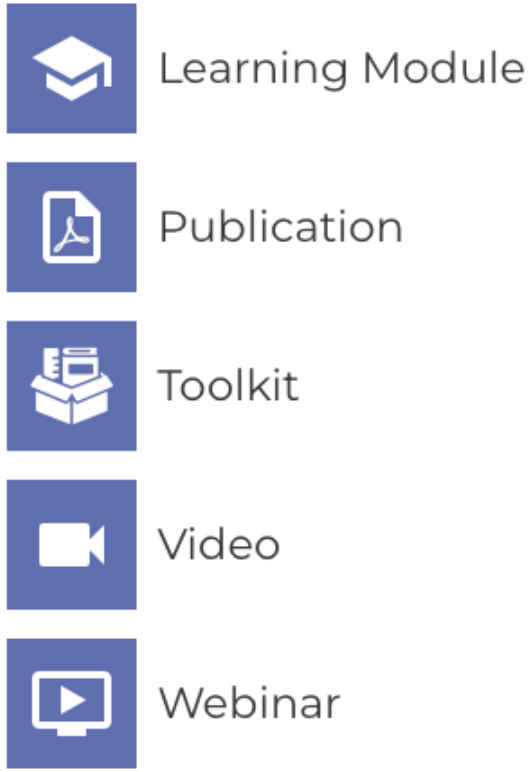
- Independent 501(c)(3) FQHC
- Founded 1971
- Mission: To enhance the wellbeing of the LGBTQIA+ community as well as people in our neighborhoods and beyond through access to the highest quality health care, education, research, and advocacy
- Integrated primary care model, including HIV and transgender health services

The Fenway Institute

- Research, Education, Policy

The National LGBTQIA+ Health Education Center

- Training and Technical Assistance
- Grand Rounds
- Online Learning
  - CE and HEI Credit
- Environmental Influences On Child Health Outcomes (ECHO) Programs
- Publications and Resources



www.lgbtqiahealtheducation.org

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- Alternatively, e-mail us at education@fenwayhealth.org for less urgent questions.

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- Choose “I will call in”
- Dial the phone number and access code

CME/CEU Information

Physicians	AAFP Prescribed credit is accepted by the American Medical Association as equivalent to AMA PRA Category 1 Credit™ toward the AMA Physician's Recognition Award. When applying for the AMA PRA, Prescribed credit earned must be reported as Prescribed, not as Category 1.
Nurse Practitioners, Physician Assistants, Nurses, Medical Assistants	AAFP Prescribed credit is accepted by the following organizations. Please contact them directly about how participants should report the credit they earned. • American Academy of Physician Assistants (AAPA) • National Commission on Certification of Physician Assistants (NCCPA) • American Nurses Credentialing Center (ANCC) • American Association of Nurse Practitioners (AANP) • American Academy of Nurse Practitioners Certification Program (AANPCP) • American Association of Medical Assistants (AAMA)
Other Health Professionals	Confirm equivalency of credits with relevant licensing body.

Learning objectives

1. Describe the indications for and options available for HIV prevention with antiretroviral medications.
2. Summarize an approach to identifying the best prevention options for a range of patients and demonstrate how to have a shared decision-making conversation about HIV prevention.
3. Understand what is on the horizon for HIV prevention in the United States.

Case

A 27-year-old man presents requesting PrEP.

He is overweight (BMI 29.4) but has no other chronic medical problems and takes no medications.

He has had condomless insertive/receptive anal sex with two men in the past 6 months.

Three months ago, he was treated for pharyngeal gonorrhea.

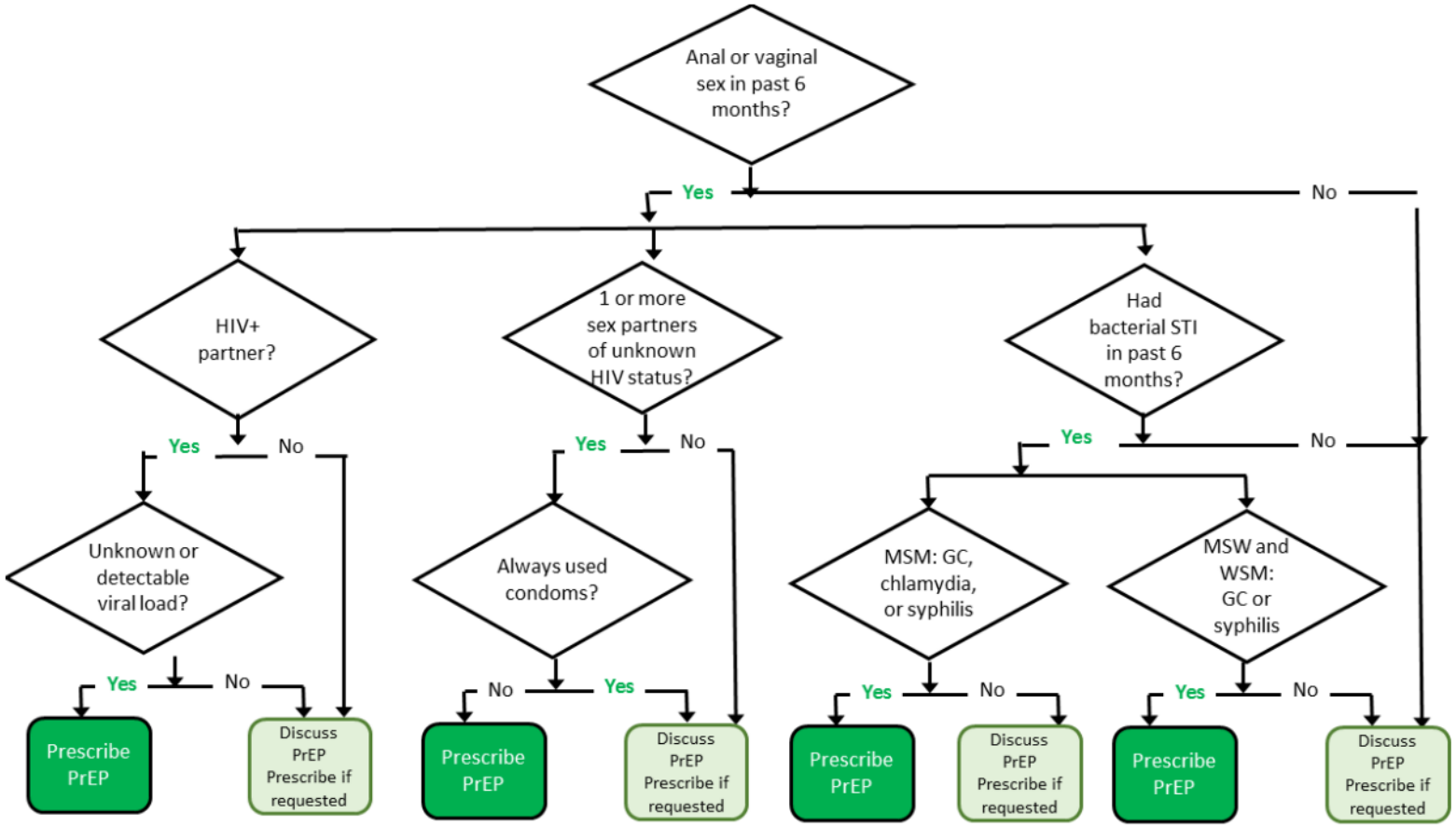
Questions

How would you approach PrEP for this patient?

Eligibility?
Baseline testing?
Medication options?
Adherence support?

PrEP indications for sexually active people

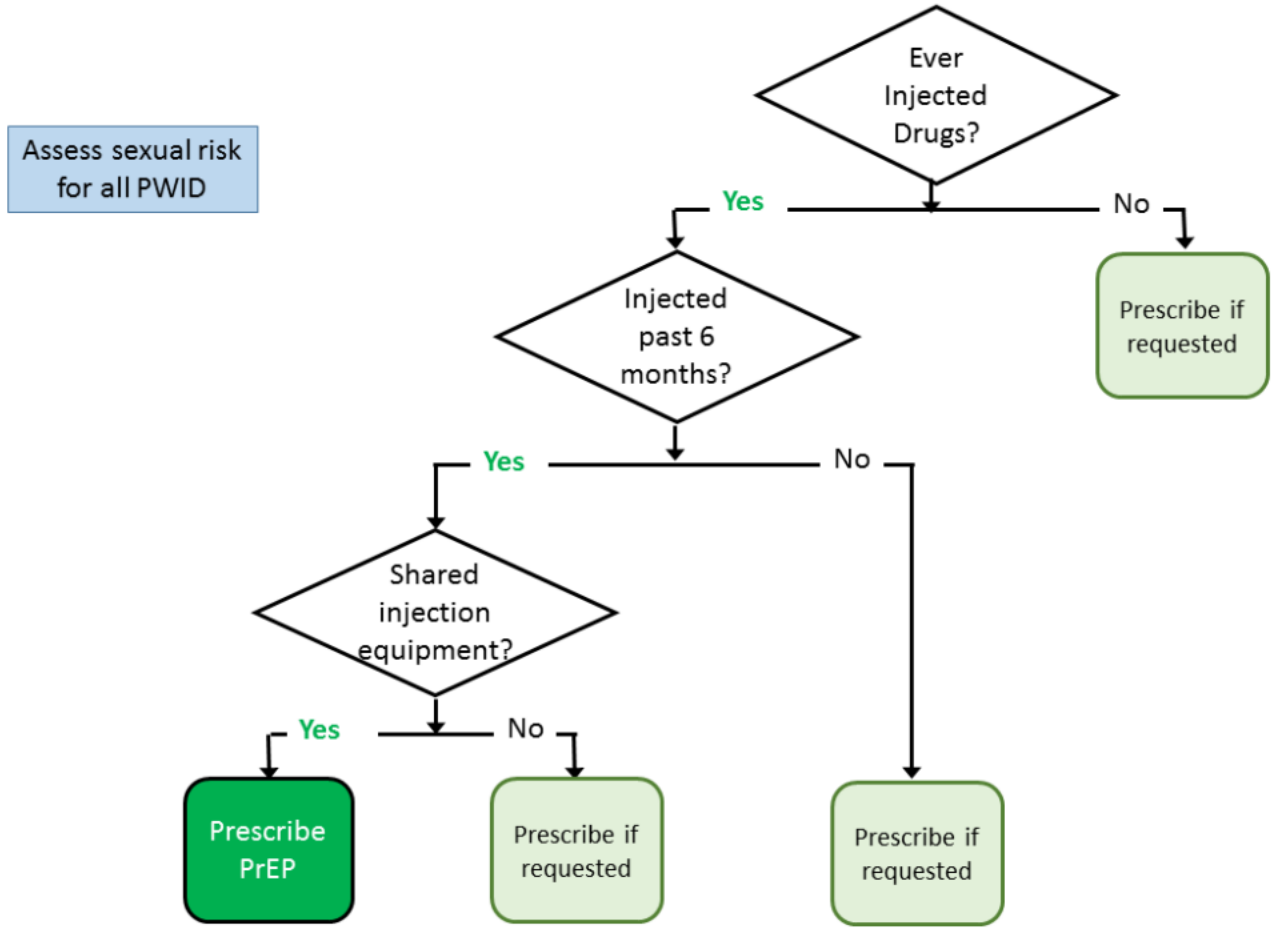
Figure 2 Assessing Indications for PrEP in Sexually Active Persons



Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 update: a clinical practice guideline. 2021. Available at: https://stacks.cdc.gov/view/cdc/112360

PrEP indications for people who inject drugs

Figure 3 **Assessing Indications for PrEP in Persons Who Inject Drugs**



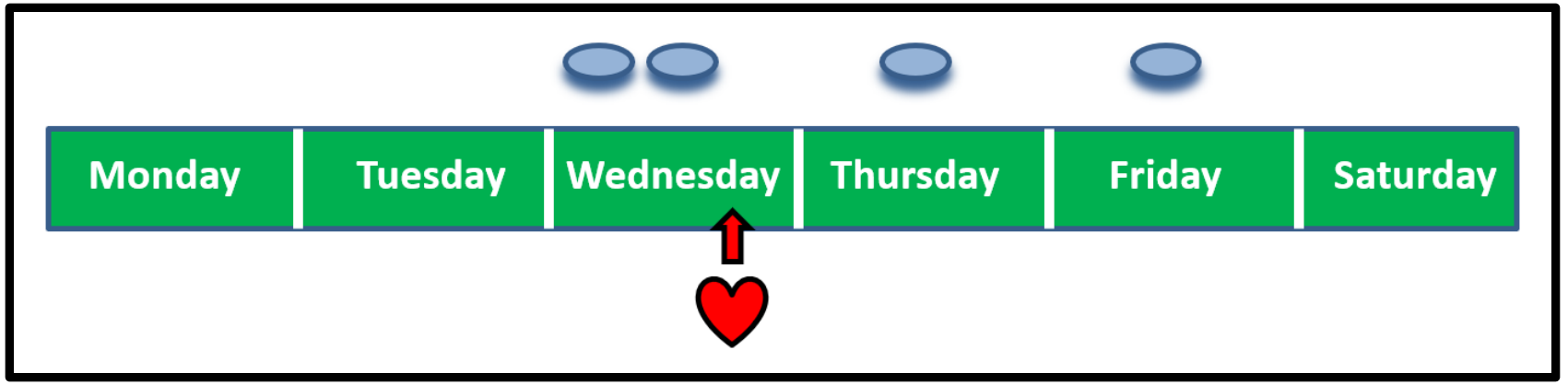
Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 update: a clinical practice guideline. 2021. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

TDF/FTC

- **Evidence:** Prevents HIV acquisition through sex and injection drug use; efficacy has been demonstrated among a broad range of people
- **Dosing:** One tablet (emtricitabine [FTC] 200 mg and tenofovir disoproxil fumarate [TDF] 300 mg) once daily*
- **Advantages:**
  - Longest clinical experience among PrEP agents, including in pregnancy
  - Available as a generic
  - Can be used in an on-demand fashion by MSM*
- **Disadvantages:**
  - Renal toxicity and decreased bone mineral density
  - Requires baseline hepatitis B testing

On-demand TDF/FTC (“2-1-1”)

- Considered an alternative for MSM without chronic hepatitis B
- With TDF/FTC only; no published data with other PrEP agents
- Prescribe no more than 30 tablets at a time before retesting for HIV
- Follow the same laboratory monitoring strategy as for daily oral TDF/FTC



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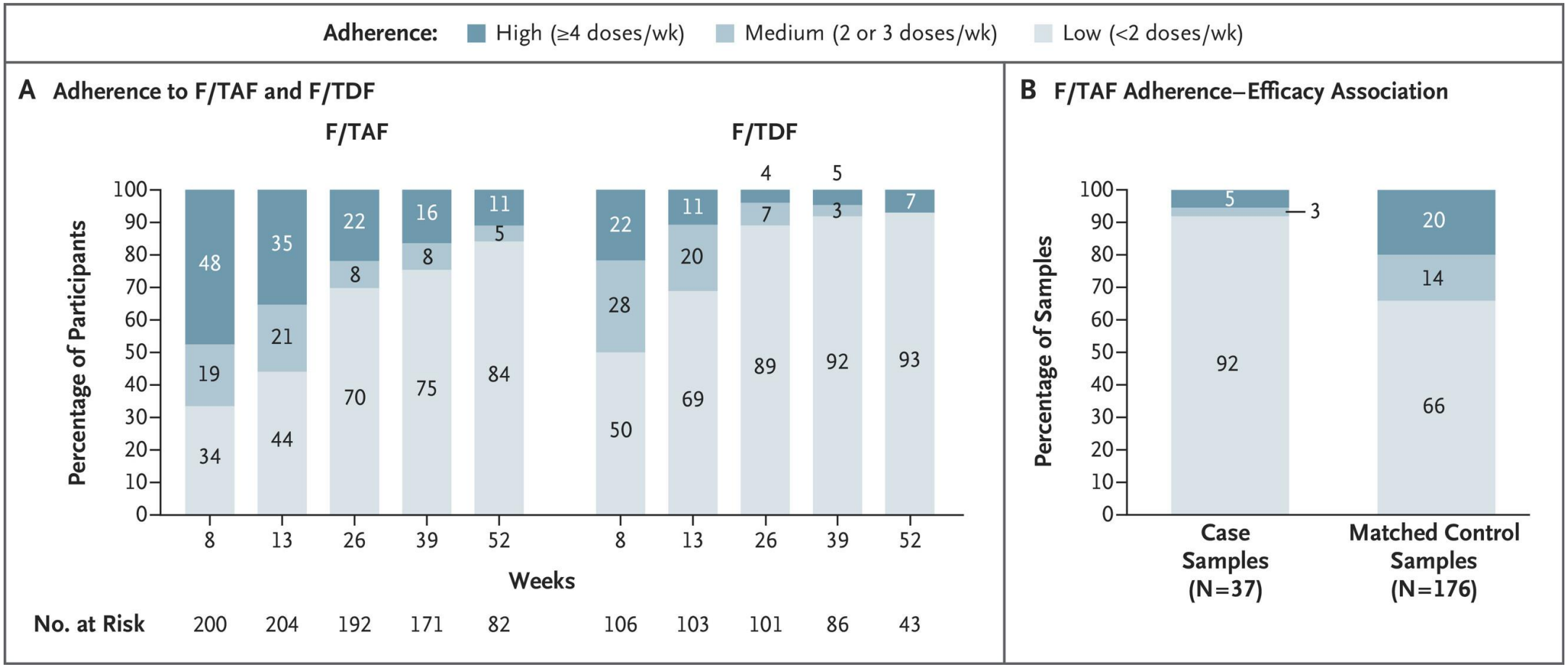
TAF/FTC

- **Evidence:** Prevents HIV acquisition through sex; non-inferior to TDF/FTC among men who have sex with men (MSM)
- **Dosing:** One tablet (emtricitabine [FTC] 200 mg and tenofovir alafenamide [TAF] 25 mg) once daily
- **Advantages:**
  - Fewer renal and bone effects in comparison to TDF/FTC
- **Disadvantages:**
  - Efficacy for people whose HIV risk arises from receptive vaginal sex is unknown
  - Has mild deleterious effects on lipids and weight
  - Requires baseline hepatitis B testing

TAF/FTC prevents HIV among women with high adherence.



Bekker LG, N Engl J Med, 2024

Laboratory monitoring for oral PrEP

Test	Screening/Baseline Visit	Q 3 months	Q 6 months	Q 12 months	When stopping PrEP
HIV Test	X*	X			X*
eCrCl	X		If age ≥50 or eCrCL <90 ml/min at PrEP initiation	If age <50 and eCrCl ≥90 ml/min at PrEP initiation	X
Syphilis	X	MSM /	X		MSM/
Gonorrhea	X	MSM /	X		MSM
Chlamydia	X	MSM /	X		MSM
Lipid panel (F/TAF)	X			X	
Hep B serology	X				
Hep C serology	MSM, and PWID only			MSM, and PWID only	

* Assess for acute HIV infection (see Figure 4)

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 update: a clinical practice guideline. 2021. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

Cabotegravir (CAB)

- **Evidence:** Prevents HIV acquisition through sex; superior to TDF/FTC for PrEP among MSM, women, and others
- **Dosing:**
  - Cabotegravir 600 mg intramuscularly once monthly for 2 doses, then every 2 months
  - An oral lead-in phase of cabotegravir 30 mg once daily prior to the first injection is optional.
- **Advantages:**
  - Obviates the need for daily pill adherence
  - Superior to TDF/FTC for PrEP in a range of populations
- **Disadvantages:**
  - Injection site reactions are common, although often mild.
  - Benefits navigation may be time-consuming.
  - Same-day initiation may not be possible currently.
  - Implications of the medication's tail phase
  - If HIV occurs despite CAB, HIV test interpretation may be challenging.

Laboratory monitoring for cabotegravir

Test	Initiation Visit	1 month visit	Q2 months	Q4 months	Q6 months	Q12 months	When Stopping CAB
HIV*	X	X	X	X	X	X	X
Syphilis	X	[redacted]	[redacted]	MSM^/[redacted] only	Heterosexually active women and men only	X	MSM/[redacted] only
Gonorrhea	X	[redacted]	[redacted]	MSM/[redacted] only	Heterosexually active women and men only	X	MSM/[redacted] only
Chlamydia	X	[redacted]	[redacted]	MSM/[redacted] only	MSM/[redacted] only	Heterosexually active women and men only	MSM/[redacted] only

* HIV-1 RNA assay

X all PrEP patients

^ men who have sex with men

[redacted]

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 update: a clinical practice guideline. 2021. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

The IAS-USA no longer recommends HIV RNA assays for PrEP monitoring.

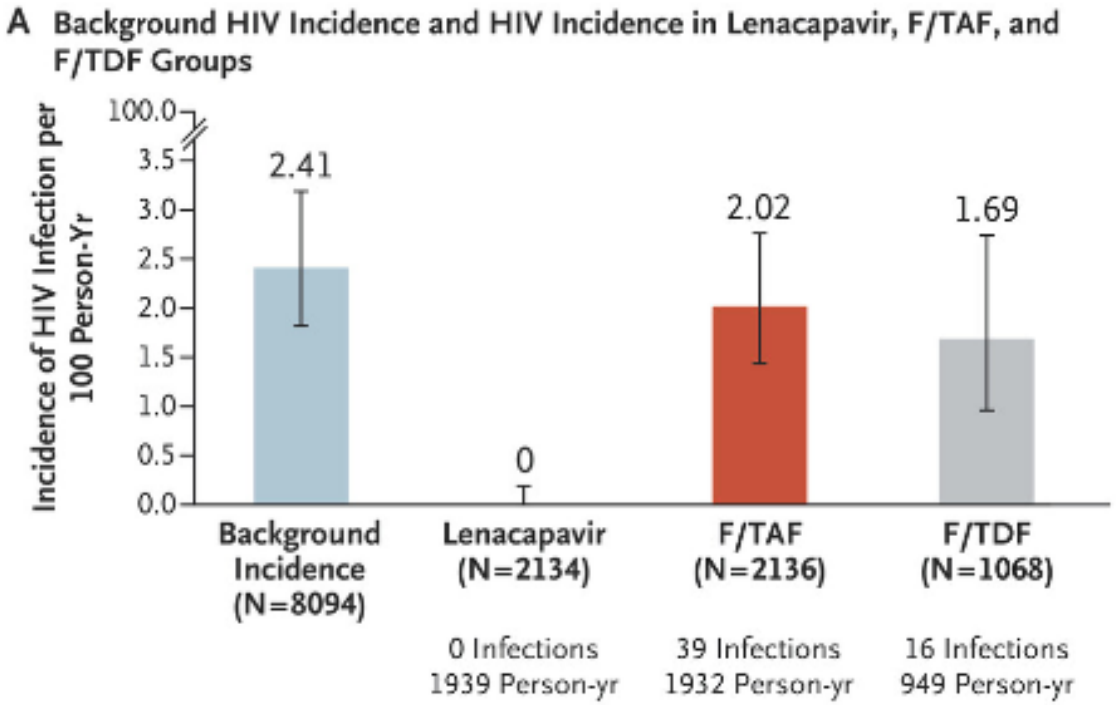
"Follow up testing for cabotegravir PrEP breakthrough infections should not routinely include HIV RNA testing but should include a point-of-care rapid HIV antibody test and a laboratory-based antigen/antibody test. RNA testing as part of routine monitoring for PrEP failure is not recommended because such testing has a low positive predictive value and false-positive results have significant negative sequelae."

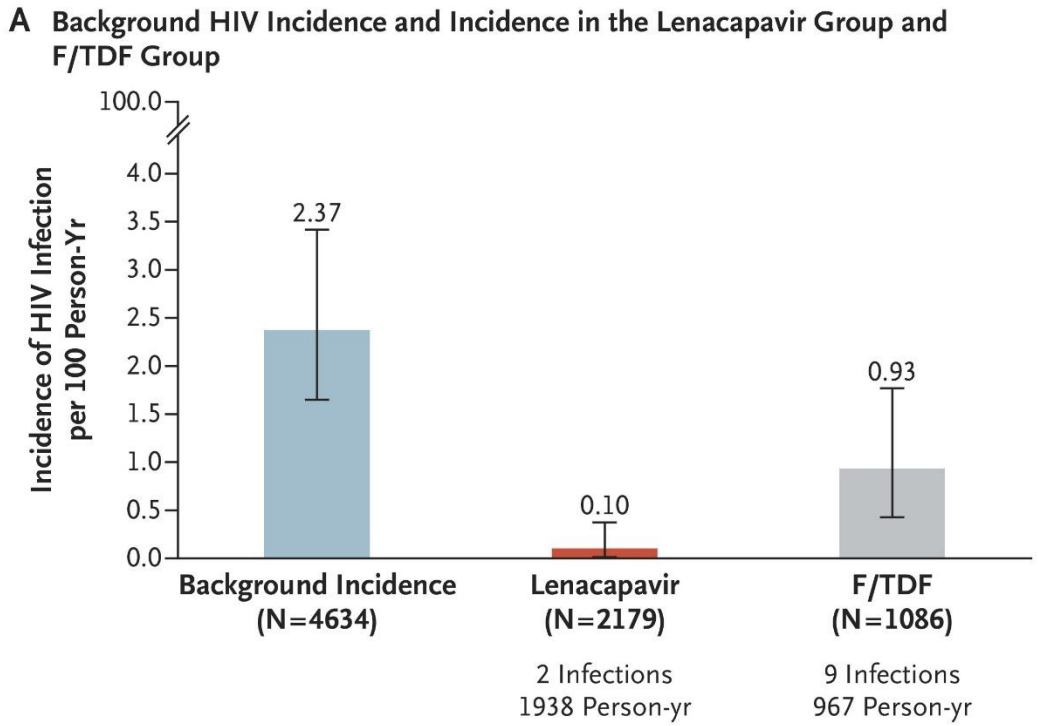
Gandhi RT, JAMA, 2024

Lenacapavir (LEN)

- **Evidence:** Prevents HIV acquisition through sex among a broad range of people
- **Dosing:**
  - Lenacapavir 927 mg subcutaneously every 26 weeks (+/- 2 weeks)
  - Lenacapavir 600 mg by mouth daily for 2 days with initiation of the drug
- **Advantages:**
  - Infrequent dosing interval
  - Superior to TDF/FTC for PrEP in a range of populations
  - Can be used in pregnancy
- **Disadvantages:**
  - Injection site reactions are common, although often mild.
  - Benefits navigation may be time-consuming.
  - Same-day initiation may not be possible currently.
  - Implications of the medication's tail phase
  - Drug-drug interactions

Evidence for Lenacapavir





Bekker LG, N Engl J Med, 2024; Kelley CF, N Engl J Med, 2024

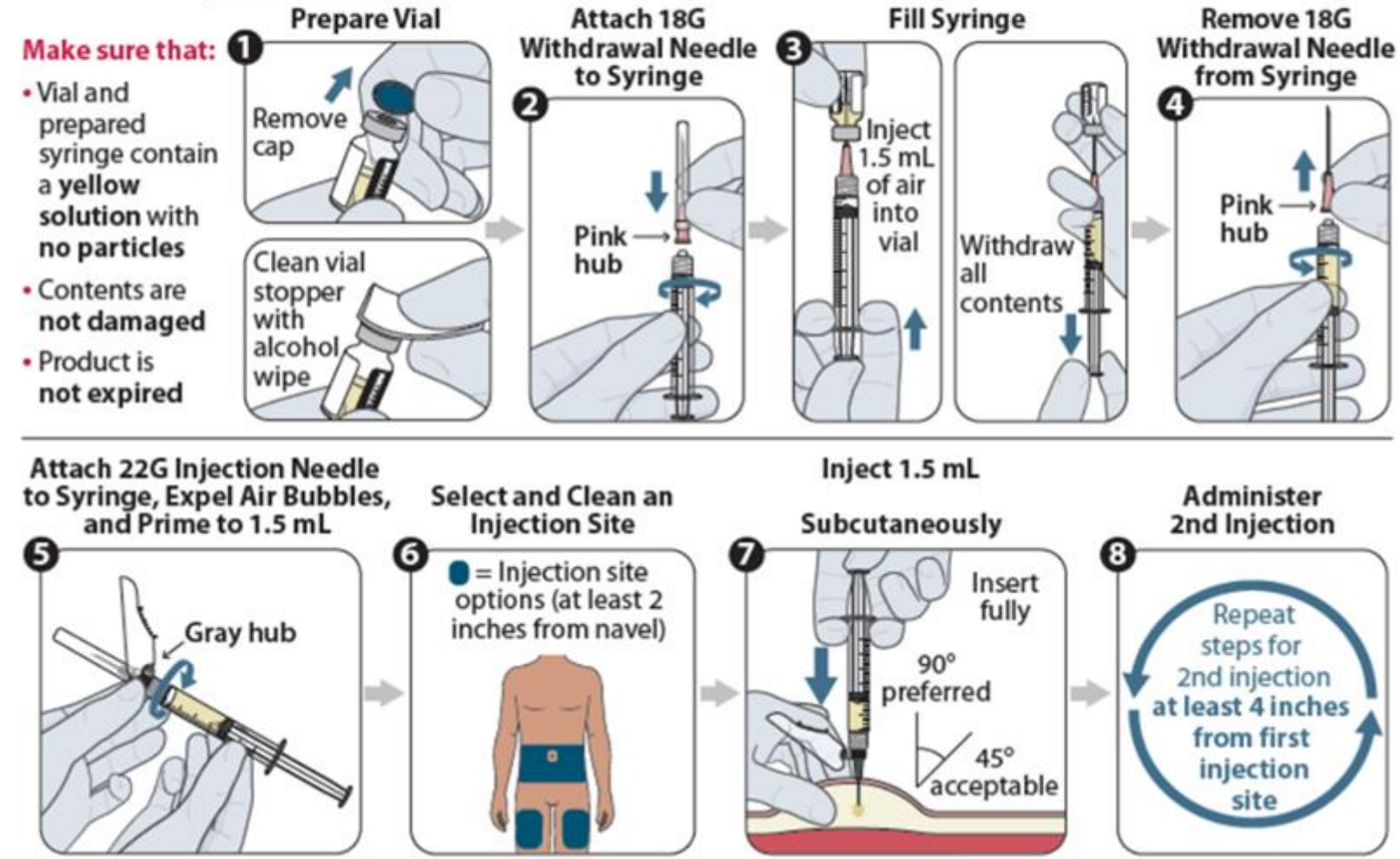
Injection site reactions

- Reported by a majority of people receiving lenacapavir in the Purpose 1 and Purpose 2 trials
- Generally mild to moderate
- Subcutaneous nodules common, with a median duration of 183 days and a median diameter of 3 cm
- Keloid formation not reported
- Reports of injection site reactions diminish with time on the drug

Administration, monitoring, and logistics

- **Baseline testing:** HIV antibody/antigen test and HIV RNA (though the latter can be pending when the first dose is administered)
- **Initiation:**
  - Day 1: 927 mg SC (two 1.5 mL injections) and 600 mg by mouth (two 300 mg tablets)
  - Day 2: 600 mg by mouth (two 300 mg tablets)
- **Continuation injections:**
  - HIV antibody/antigen test (if rapid, should be confirmed with a lab-based test)
  - 927 mg SC every 26 weeks (+/- 2 weeks)
- **Drug interactions:** With moderate or strong CYP3A inducers, supplemental doses of lenacapavir may be required

Figure 2 **Injection Steps for Withdrawal Needle Injection Kit**



www.accessdata.fda.gov/drugsatfda_docs/label/2025/220020s000lbl.pdf

Anticipated delayed injections

Table 2. Dosing Schedule for Anticipated Delayed Injections: Weekly Oral Dosage

Time since Last Injection	Dosage
26 to 28 weeks	Oral dosage of 300 mg taken once every 7 days.[a] Resume the continuation injection dosage within 7 days after the last oral dose.

a. Use on an interim basis only (for up to 6 months if needed).

www.accessdata.fda.gov/drugsatfda_docs/label/2025/220020s000lbl.pdf

Updated guidelines from the IAS-USA

- Published June 27, 2025
- Include additional sites of injection (upper gluteus, posterior upper arm)
- Mitigate injection site reactions by icing or topical analgesia
- HIV RNA monitoring for PrEP failure is not recommended
- Lenacapavir is recommended for prevention of HIV among in pregnancy
- TAF/FTC now recommended for HIV prevention among people having vaginal sex if TDF/FTC is contraindicated or undesirable

Landovitz RJ, JAMA, 2025

Updated guidelines from CDC

- Made a strong recommendation with high certainty of evidence for lenacapavir as an option for PrEP
- If HIV RNA testing is not available at initiation, repeat an HIV antibody/antigen test in 4 weeks
- Do not use oral HIV antibody tests to monitor PrEP
- If switching from another PrEP agent without interruption, only an laboratory-based HIV antibody/antigen test is required for lenacapavir initiation
- Ensure hepatitis B status is known if switching off of tenofovir-based PrEP

Patel RR, MMWR, 2025

Considerations for selecting an agent for PrEP

What do they prefer?	Comorbidities	Nature of HIV exposure	Logistics
Which PrEP agent do they want, and why?	Renal or bone disease favors TAF/FTC, CAB, or LEN	Evidence for the role of TAF/FTC for people who have receptive vaginal sex is more limited	A desire for telehealth/limited in-person visits favors oral PrEP
	Hepatitis B favors oral PrEP?	TDF is the only agent studied among people who inject drugs thus far	On-demand dosing favors TDF/FTC
	Hyperlipidemia, weight concerns favor TDF/FTC		Same-day initiation favors oral PrEP
	Drug-drug interactions may complicate use of CAB or LEN		Insurance considerations may favor a specific agent

Case

A 27-year-old man presents requesting PrEP.

He is overweight (BMI 29.4) but has no other chronic medical problems and takes no medications.

He has had condomless insertive/receptive anal sex with two men in the past 6 months.

Three months ago, he was treated for pharyngeal gonorrhea.

Case, continued

The patient and clinician decide to initiate lenacapavir for PrEP as well as doxycycline post-exposure prophylaxis for STIs.

How often should the patient return for STI testing?

STI screening on Lenacapavir

Counsel individuals on the use of other prevention measures (e.g., consistent and correct condom use; knowledge of partner(s)' HIV-1 status, including viral suppression status; regular testing for STIs that can facilitate HIV-1 transmission). Inform individuals about and support their efforts in reducing sexual behaviors associated with HIV-1 acquisition risk.

- IAS-USA guidance suggests every-3-month screening for "frequently exposed" people.
- CDC guidance does not comment on the frequency of STI screening.

www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.pdf; Landovitz RJ, JAMA, 2025; Patel RR, MMWR, 2025

Every-6-month STI testing is non-inferior to every-3-month testing among MSM.

Population: 428 MSM taking PrEP in the Netherlands

Design: Randomized trial of STI screening every 3 or 6 months

Outcomes: Additional visits rates and STI positivity

Results:

- Overall, the visit rate was lower in the 6-month group, though additional STI visits were more frequent
- There was no difference in STI positivity between groups (22% in the 6-month group and 21% in the 3-month group, P=0.35)

Some settings have reduced the frequency of STI testing for people taking PrEP.

Public Health – Seattle & King County
Preexposure Prophylaxis (PrEP) Implementation Guidelines 2025

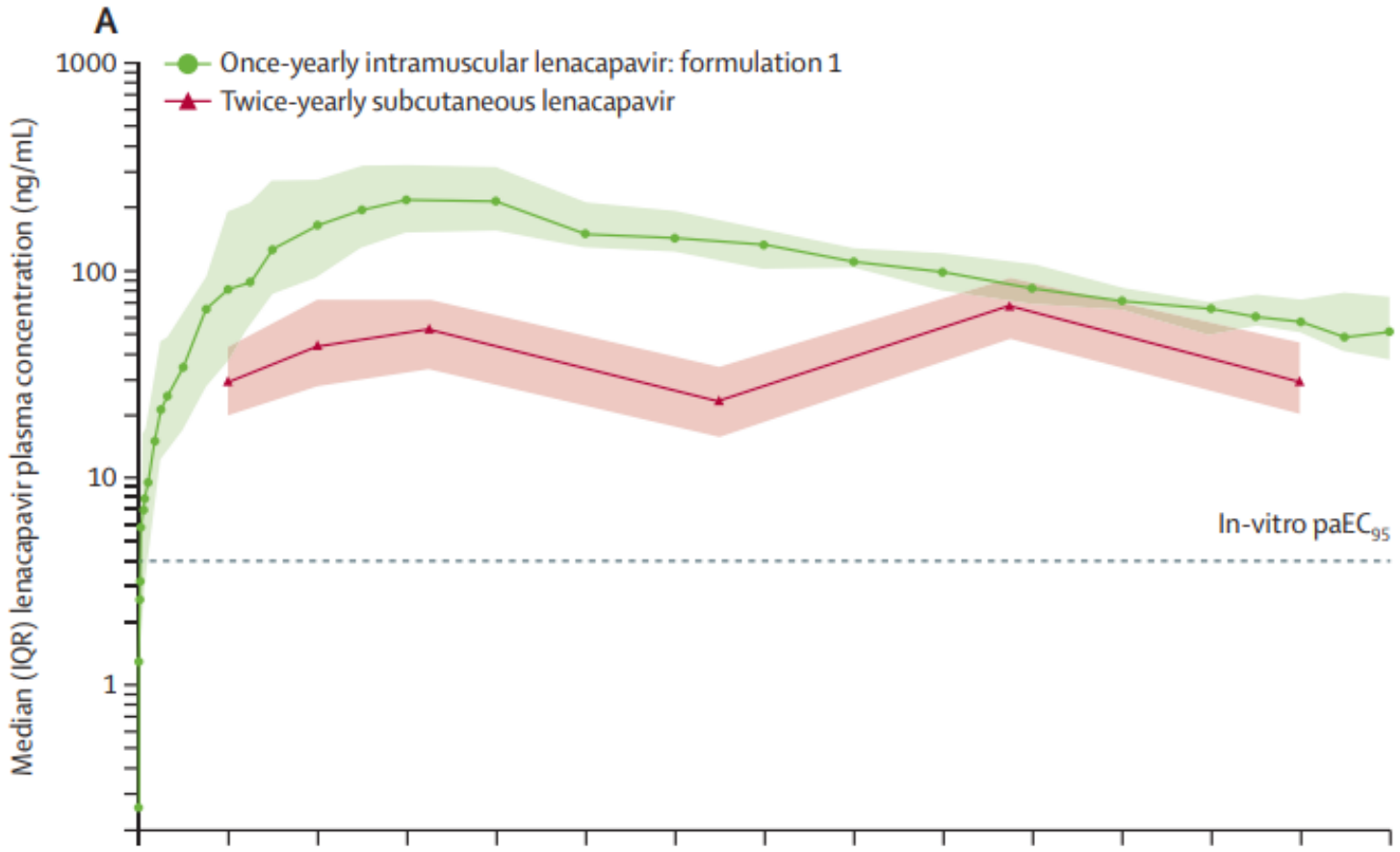
These guidelines update PHSKC guidance issued in 2024 related to HIV PrEP implementation and are designed to complement the US Public Health Service and IAS-USA PrEP guidelines.[1,2] They reflect information that was not available when national guidelines were developed as well as issues related to cost, local epidemiology, and implementation. Important changes from the 2024 guidelines are highlighted in Box 1.

Box 1. Interval changes from 2024 guidelines

- HIV and syphilis screening interval extended to 6 months for most oral PrEP users on a stable oral PrEP regimen for ≥6 months
- Recommendation not to stop PrEP in patients who do not follow up as recommended
- Routine screening for asymptomatic gonorrhea and chlamydial infection is no longer recommended in people without a uterus who have sex with men. PHSKC advises medical providers to discuss gonorrhea and chlamydial screening with patients and use shared decision-making to decide whether to screen asymptomatic people for these infections. This change is based on:
  - The absence of known sequelae associated with asymptomatic infections,
  - The fact that these infections are self-limited in the absence of treatment,
  - The uncertain impact of screening on population-level STI incidence, and
  - To avoid the unnecessary use of antimicrobials.

https://cdn.kingcounty.gov/-/media/king-county/depts/dph/documents/health-safety/disease-illness/hiv-sti/prep-implementation-guidelines.pdf?rev=3f2fc1404af94e8089a392a0a3fa6d14

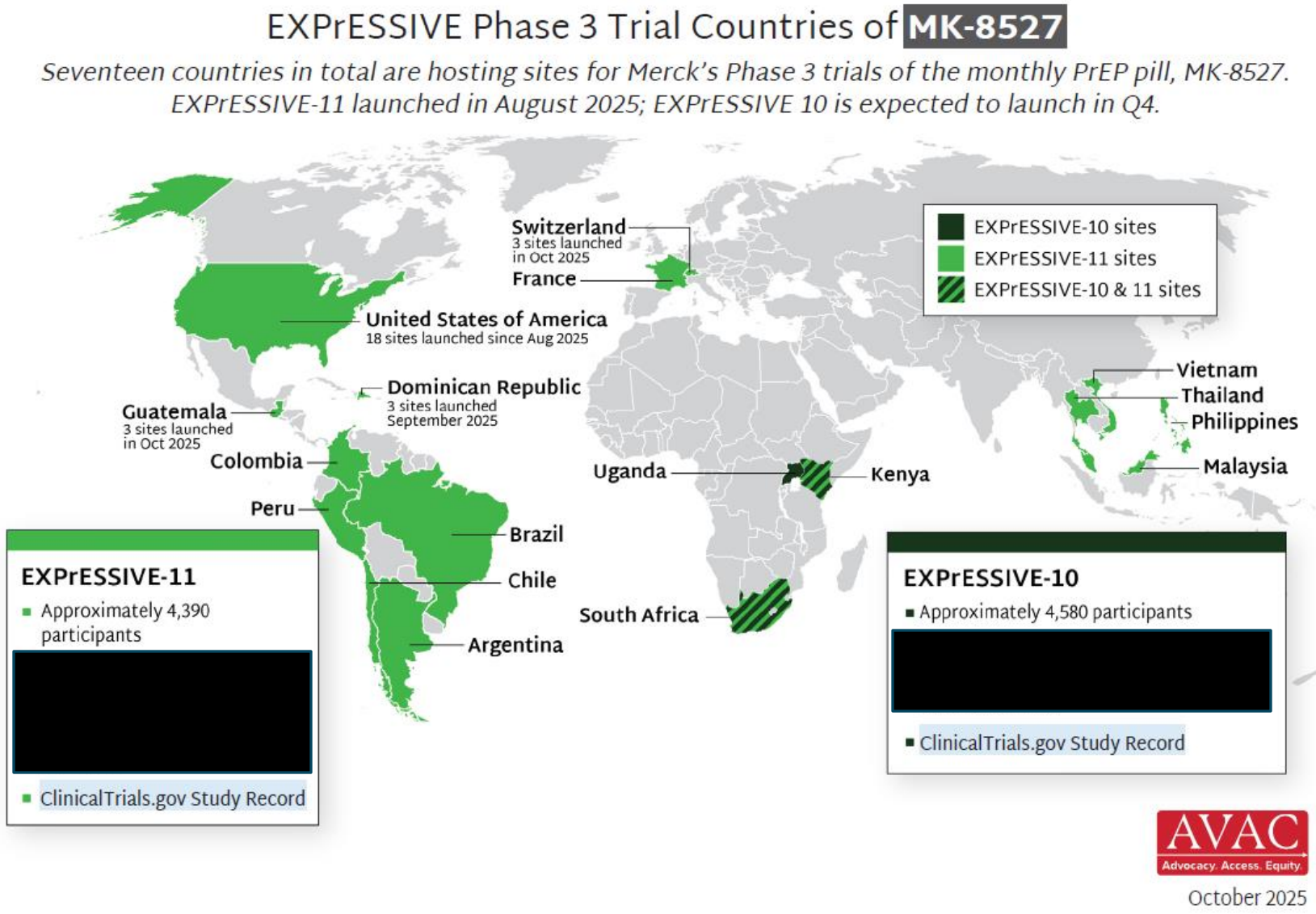
On the horizon: Once-yearly Lenacapavir?



Jogiraju V, Lancet, 2025

On the horizon: A once-monthly pill?

https://avac.org/resource/infographic/trials-countries-mk8527/



Summary

- Use of antiretrovirals as PrEP can significantly reduce the risk of HIV acquisition.
- Four options are currently available for PrEP: TDF/FTC, TAF/FTC, CAB, and LEN.
- Selection of a medication for a patient hinges on preferences, comorbidities, the nature of HIV exposure, and logistics.
- Long-acting options for PrEP may foster an already-brewing shift in STI screening frequency for people taking PrEP.

HRSA Disclaimer

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