

# 2021 PrEP Guideline Update

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**I have no financial conflicts of interest.**

# What has changed?

1. Recommendation that all sexually active people be informed about PrEP
2. PrEP indications
3. A new option: long-acting cabotegravir (CAB-LA)
4. On-demand PrEP for MSM
5. Same-day PrEP
6. Laboratory monitoring on PrEP

**PrEP turns 10!**



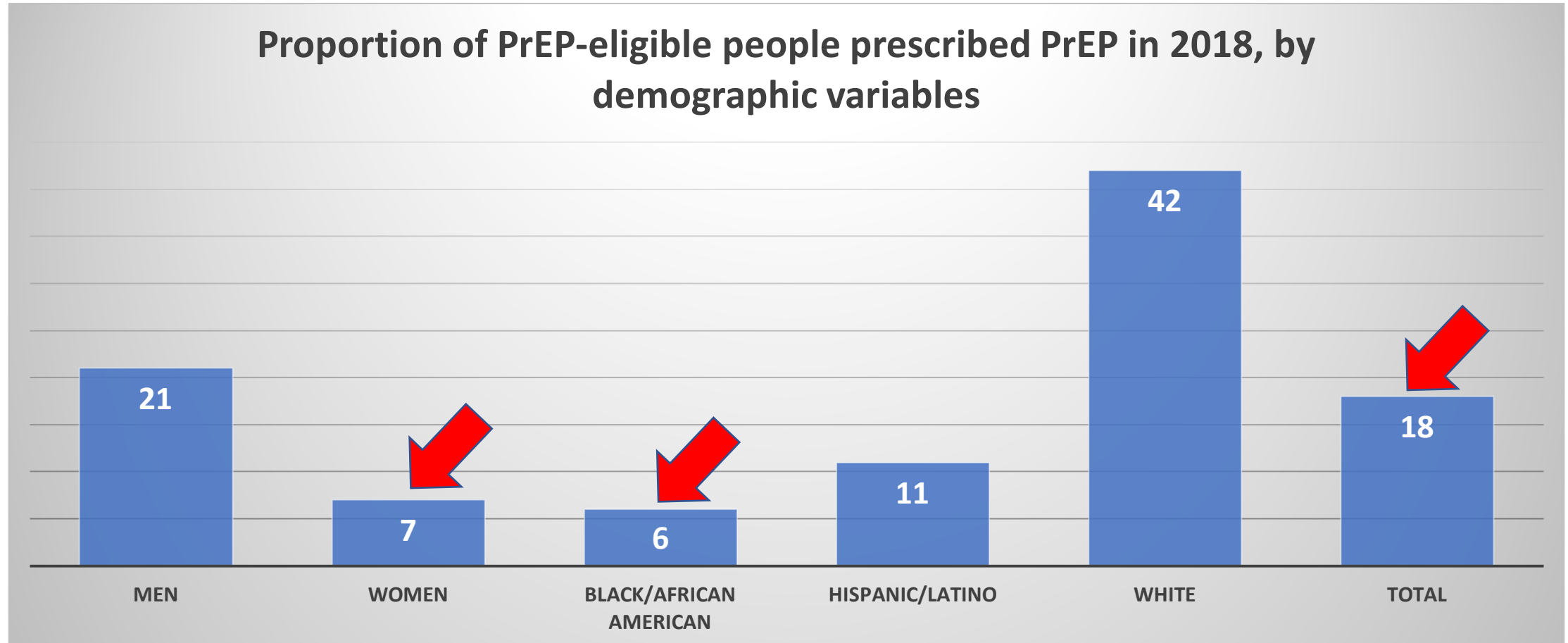
**July 16, 2022**

# Poll

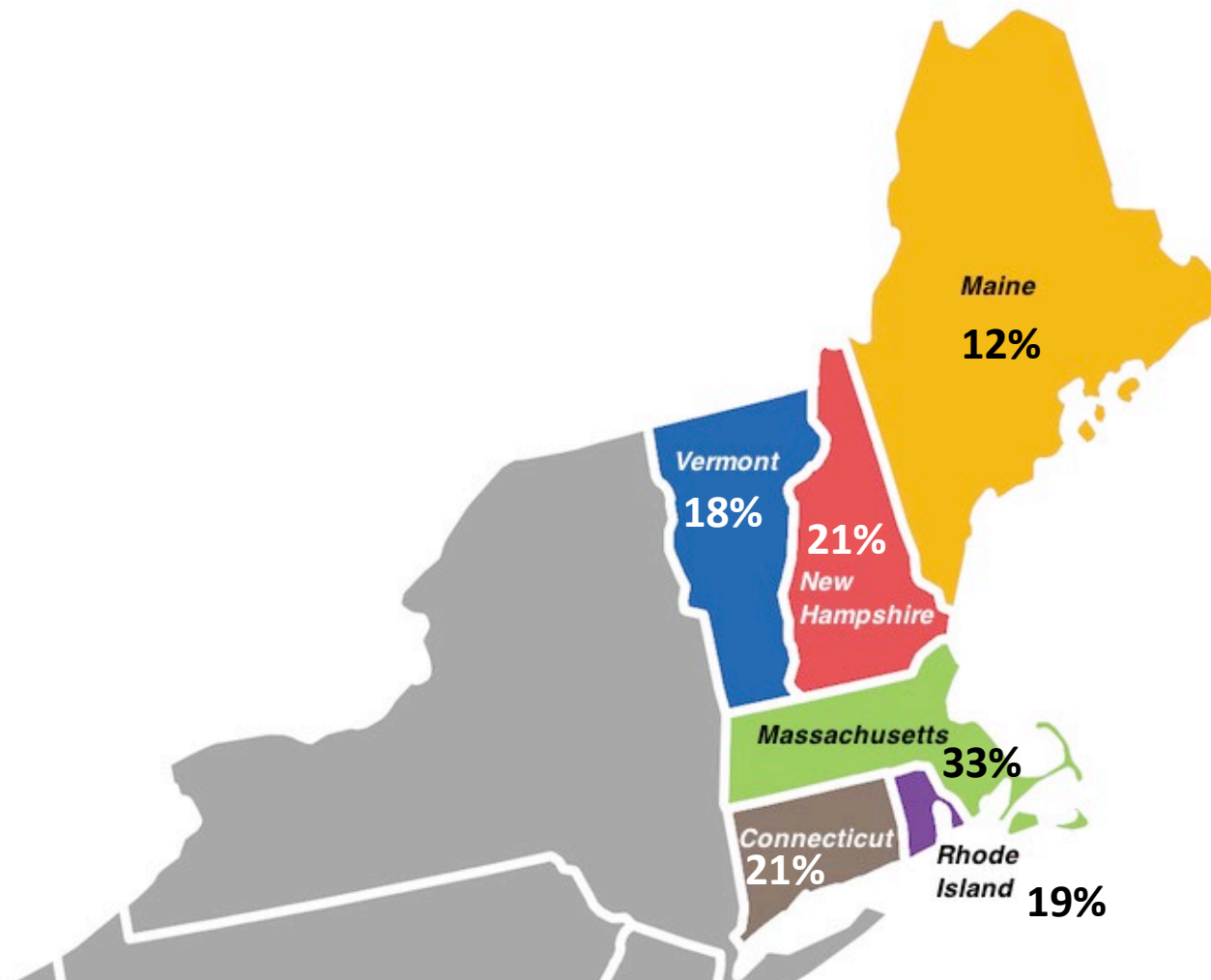
What proportion of Americans with indications for PrEP have been prescribed it?

- A. 1%
- B. 10%
- C. 20%
- D. 30%

# Most people who could benefit from PrEP are not taking it.



# Proportion of eligible people prescribed PrEP in New England, 2018

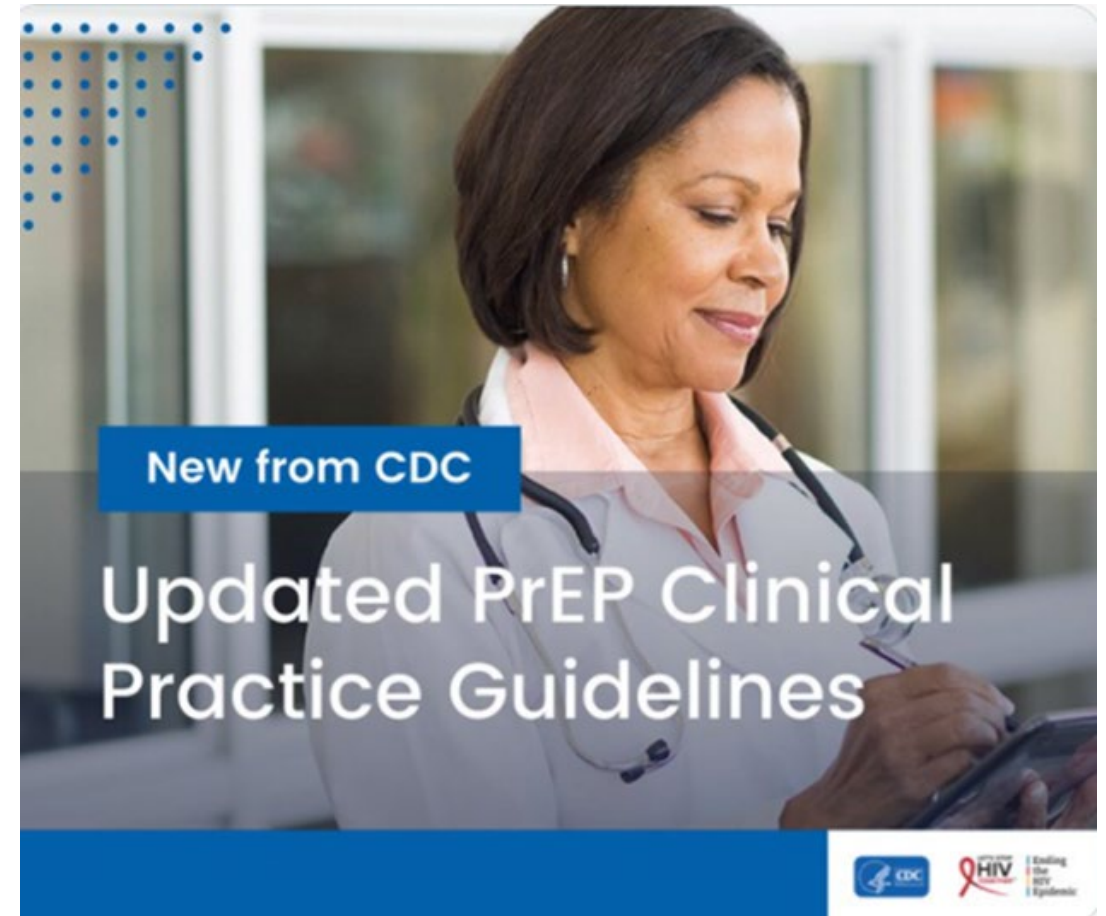


# What's Unchanged from the 2017 Guideline

## ■ No changes to:



- Indications for PrEP use
- Frequency of follow-up visits for oral PrEP
- Schedule for HIV and STI testing for oral PrEP





# PrEP indications for heterosexually active people in 2017

## BOX B2: RECOMMENDED INDICATIONS FOR PREP USE BY HETEROSEXUALLY ACTIVE MEN AND WOMEN

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

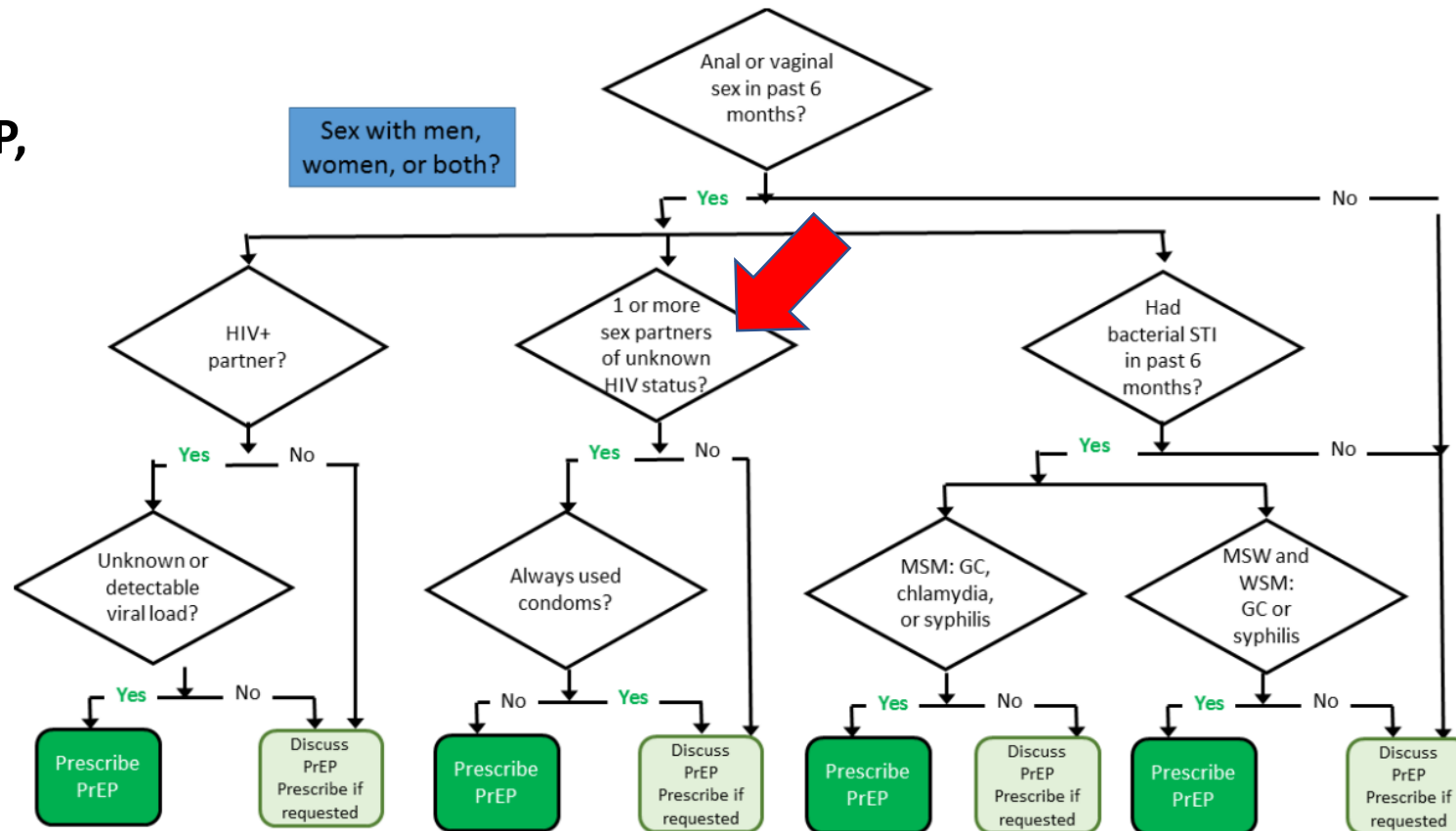
AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
- A **bacterial STI (syphilis, gonorrhea in women or men)** diagnosed or reported in past 6 months

# PrEP indications for sexually active people

Figure 2 Assessing Indications for PrEP in Sexually Active Persons

Requesting PrEP, even without reporting risks for HIV, is considered an indication for PrEP.

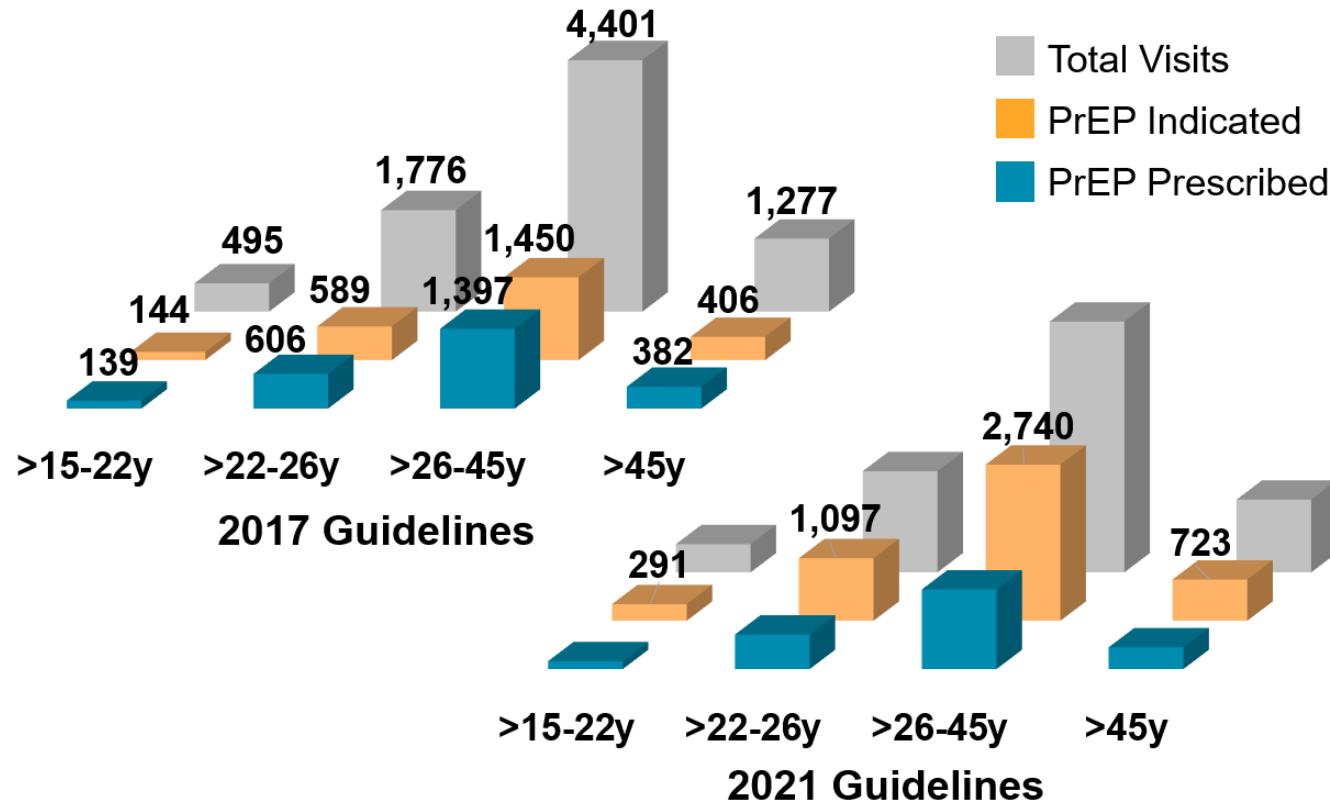


# This change increases the proportion of patients with a PrEP indication.

PrEP Cascades Based on 2017 versus 2021 CDC Guidelines, MGH Sexual Health Clinic

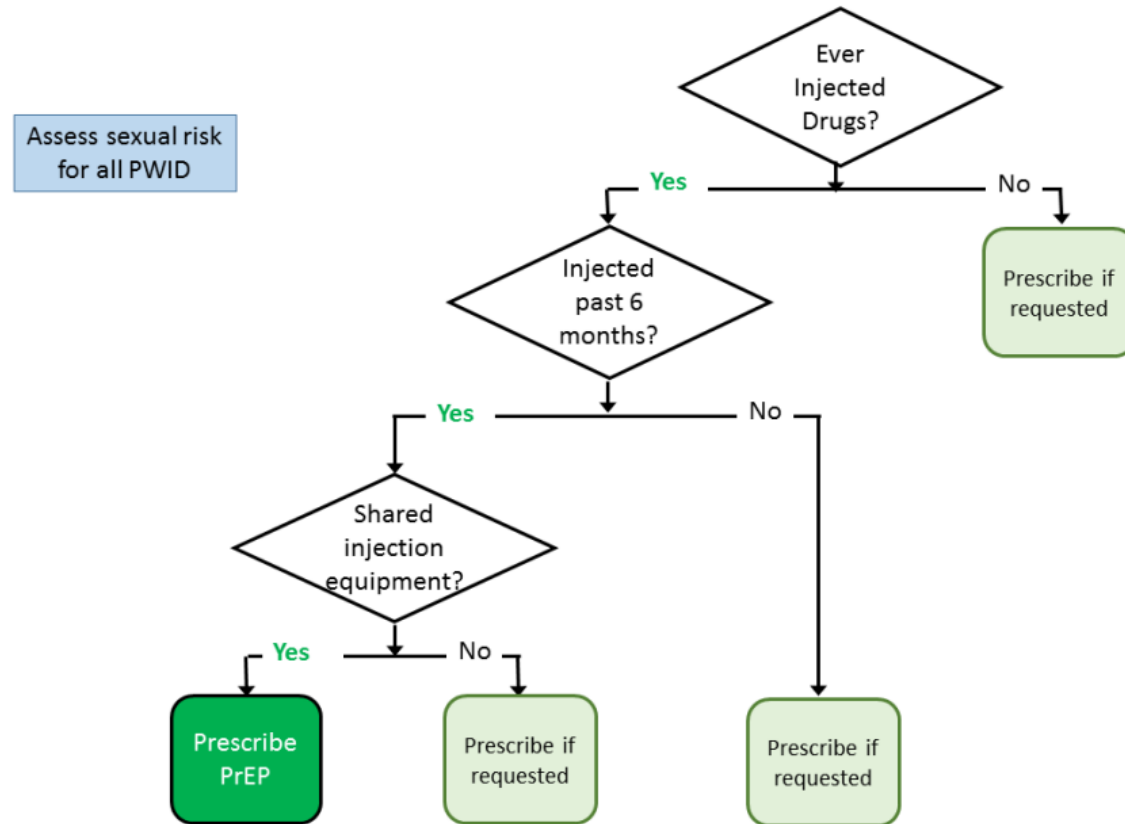
Applying the change increased the proportion of visits with a PrEP indication from 33% to 61%.

Increases were similar across age groups.



# PrEP indications for people who inject drugs

Figure 3 Assessing Indications for PrEP in Persons Who Inject Drugs



# Case

- A 27-year-old cisgender man presents in follow-up.
- He injects methamphetamine a few times each week, often sharing injection equipment with others.
- He has anal sex with cisgender men and does not use condoms.
- 2 months ago, he was diagnosed with early latent syphilis and was treated with long-acting benzathine penicillin.
- He is prescribed oral TDF/FTC for PrEP but misses weeks of pills at a time.
- Today, he is asymptomatic, and a routine HIV antibody/antigen test and HIV RNA assay are negative.

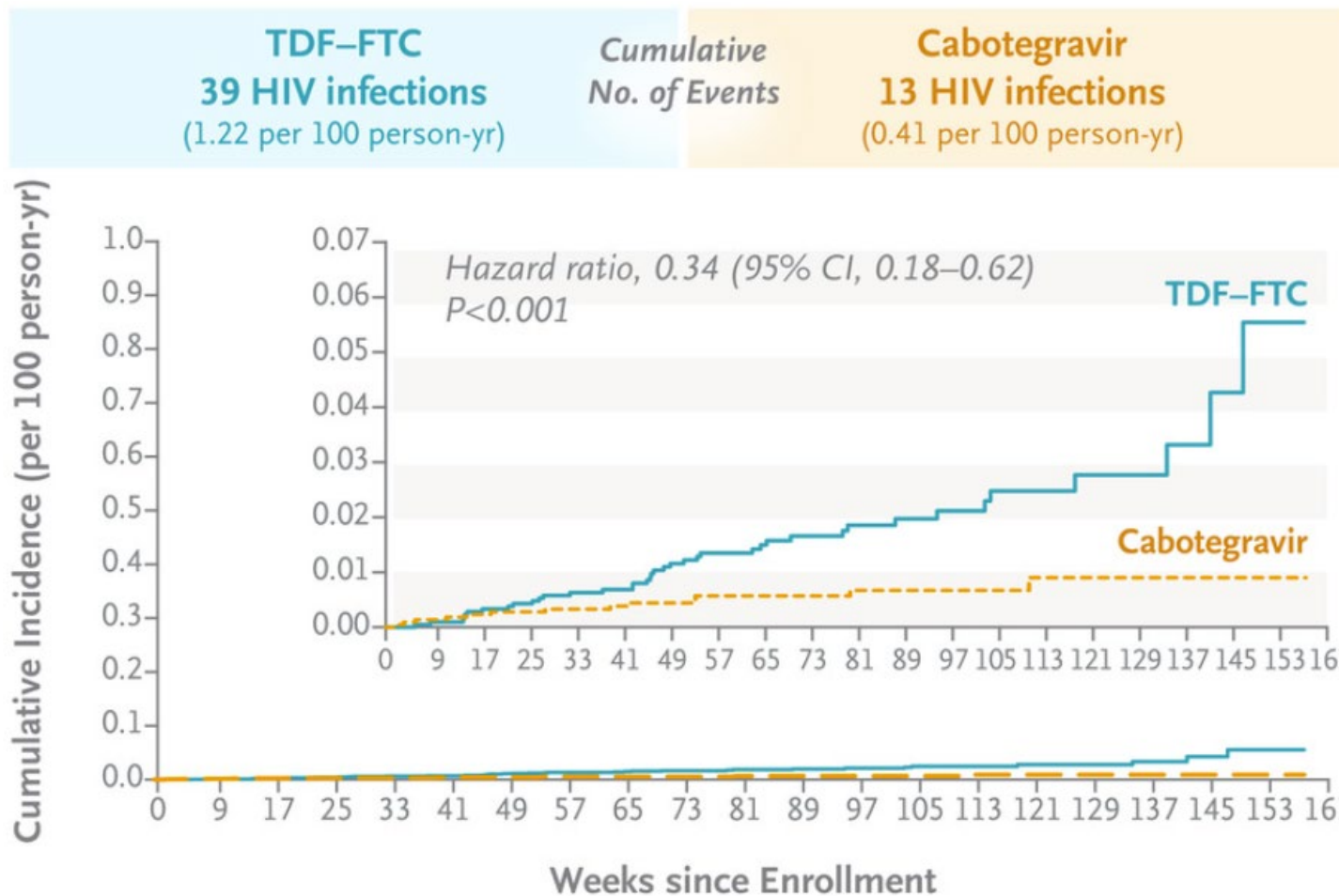
# Poll

What is the best PrEP option for him?

- A. No PrEP
- B. TDF/FTC
- C. TAF/FTC
- D. CAB-LA

# CAB-LA is superior to TDF/FTC for PrEP.

## Incident HIV Infection



# CAB-LA is superior to TDF/FTC for PrEP among cisgender women.

- **HPTN 084:** Randomized clinical trial of CAB-LA versus TDF/FTC for PrEP among 3,224 women in Africa
- CAB-LA reduced the risk of HIV by **88%** in comparison to TDF/FTC.
- Adherence to TDF/FTC was moderate; **42%** took it daily based on drug levels.

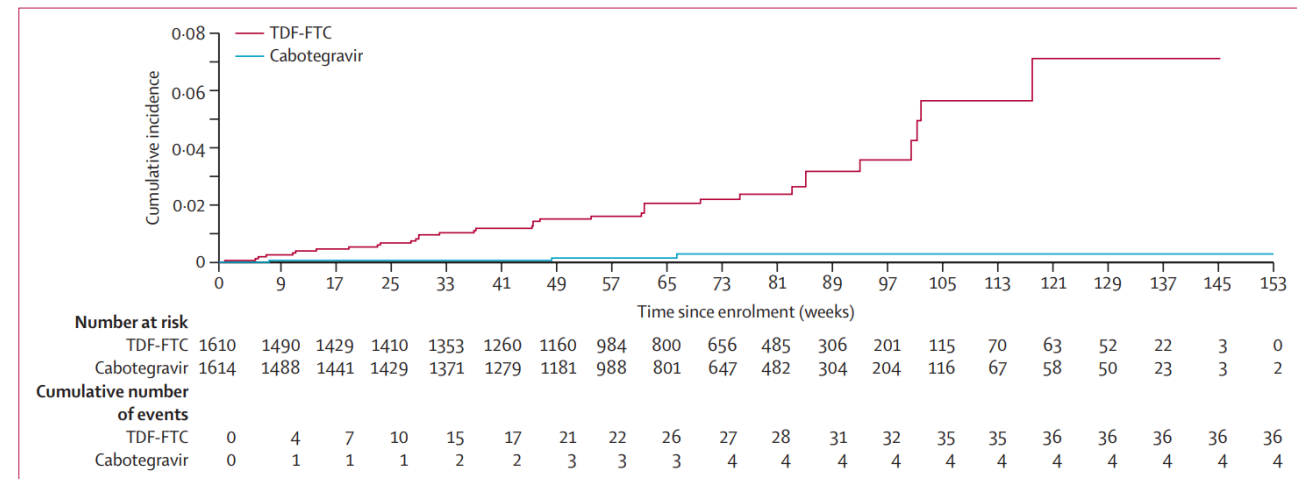


Figure 3: Cumulative HIV incidence by study group



# Questions about CAB-LA

## Will it prevent HIV transmission from injection drug use?

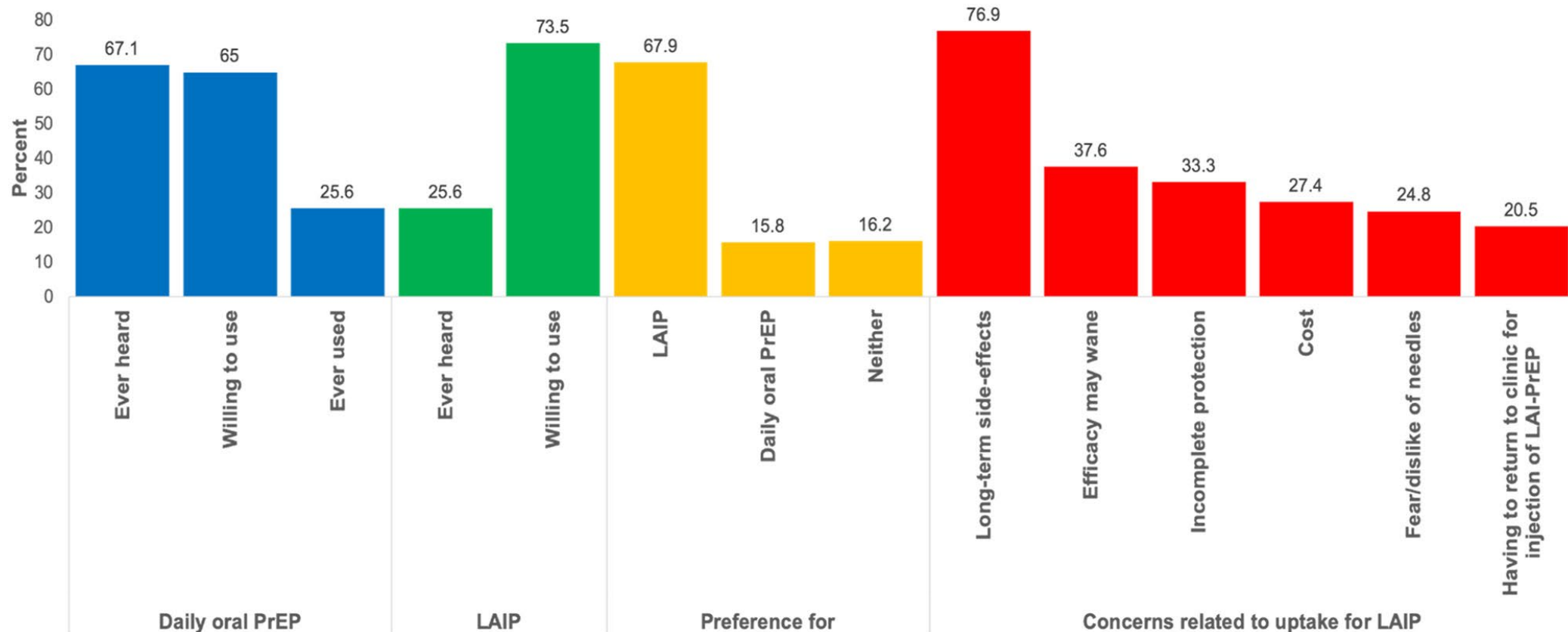
- **CDC:** “PWID are likely to benefit from PrEP with any FDA-approved medication with or without an identified sexual behavior risk of HIV acquisition.”

1. 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>.

2. FDA news release. 2021 Dec 20. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention>.

# Perceptions of long-acting injectable PrEP among people who inject drugs

Perceptions among 234 people with opioid use disorder in CT



# Questions about CAB-LA

## Will it prevent HIV transmission from injection drug use?

- **CDC:** “PWID are likely to benefit from PrEP with any FDA-approved medication with or without an identified sexual behavior risk of HIV acquisition.”

## Can CAB-LA be used in adolescents?

- The FDA approved the drug for adults *and* adolescents.
- **CDC:** “CAB is not recommended for adolescents < 18 years old.”
- The HPTN 083-01 study is assessing CAB-LA among people < 18 years.

1. 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>.

2. FDA news release. 2021 Dec 20. Available at: <https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention>.

# Questions about CAB-LA, continued

## Will CAB-LA be compatible with pregnancy/breastfeeding?

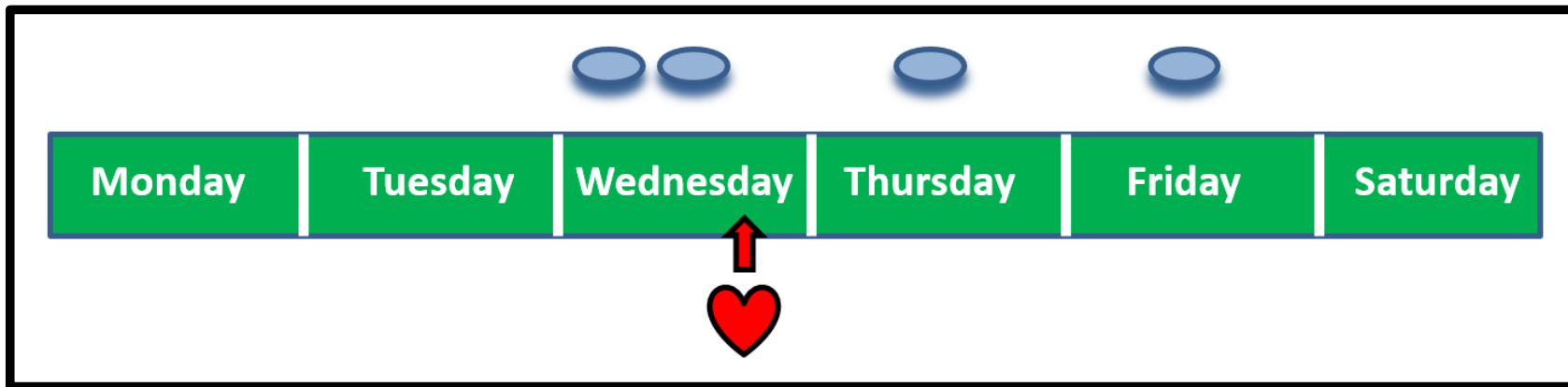
- **HPTN 084:** 29 pregnancies in the CAB-LA group; no congenital anomalies observed
- **Package insert:**
  - Use during pregnancy “only if the expected benefit justifies the potential risk to the fetus.”
  - Implications of tail phase
  - Antiretroviral Pregnancy Registry ([www.apregistry.com](http://www.apregistry.com))

# Evidence indicates no concerns with TDF/FTC during pregnancy

- DHHS guidelines recommended TDF/FTC as PrEP for people at high risk for HIV during pregnancy and breastfeeding
- In a PrEP implementation project in Kenya with 206 women using PrEP during pregnancy and 1324 not using PrEP, there were no differences in:
  - Gestational age at birth (mean 38.5 weeks)
  - Birthweight
  - Infant growth at 6 weeks post-partum

# On-demand PrEP

- Described as an alternative for MSM without chronic hepatitis B
- With TDF/FTC only; not an FDA approved strategy
- Prescribe no more than 30 tablets at a time before retesting for HIV



# Same-day PrEP is a promising strategy.

## **Panel: Considerations for same-day PrEP**

### **Reasons to consider same-day PrEP**

- Minimise drop-off between PrEP evaluation and initial prescription
- Reduce barriers to PrEP access and delivery (eg, time)
- Standard of care for other medical conditions (eg, oral contraceptives)

### **Reasons not to consider same-day PrEP**

- System barriers (absence of insurance or payment assistance, absence of referral network for PrEP continuity care, absence of laboratory services)
- Patient considerations (history of renal disease, inability to contact for follow-up if abnormal laboratory test results)
- Unknown effect on PrEP persistence and adherence

### **Facility considerations for providing same-day PrEP**

- Ability to do point-of-care HIV testing
- Ability to test for creatinine and pregnancy
- Ability to draw blood for laboratory testing
- Ability to contact patients to discontinue PrEP if needed
- Access to insurance navigation and medication assistance programmes for uninsured and underinsured individuals
- Capacity to attend the 1 month or 3 month (or both) follow-up appointments for ongoing PrEP care (onsite or through referral network)

# PrEP options in 2021

| Medication                        | Advantages  | Disadvantages   |
|-----------------------------------|---|---|
| <b>Oral TDF/FTC</b>               | <ul style="list-style-type: none"><li>→Prevents HIV acquisition through sex and injection drug use</li><li>→Effective when used in an on-demand fashion among MSM</li><li>→Available as a generic</li></ul>   | <ul style="list-style-type: none"><li>→Should not be used when estimated creatinine clearance is <math>&lt; 60</math> mL/min</li><li>→Risks of renal adverse events and decreased bone mineral density</li></ul>      |
| <b>Oral TAF/FTC</b>               | <ul style="list-style-type: none"><li>→Prevents HIV acquisition through sex</li><li>→Less likely than TDF/FTC to adversely affect kidneys or bone</li><li>→Can be used if the estimated creatinine clearance is <math>\geq 30</math> mL/min</li></ul> | <ul style="list-style-type: none"><li>→Use in an on-demand fashion or among cisgender women has not been studied</li><li>→Risk of weight gain and dyslipidemia</li></ul>  |
| <b>Intramuscular CAB (CAB-LA)</b> | <ul style="list-style-type: none"><li>→Superior to TDF/FTC for PrEP among MSM, transgender women, and cisgender women</li><li>→Every-two-month injections obviate the need for taking a pill daily</li></ul>  | <ul style="list-style-type: none"><li>→Requires more frequent clinic visits than oral PrEP</li><li>→Injection site reactions are common but tend to be mild</li><li>→Limited data about safety in pregnancy</li></ul> |



# Laboratory tests NOT routinely recommended for PrEP

DEXA

Liver enzymes

Complete blood counts

Urinalyses

**Table 5 Timing of Oral PrEP-associated Laboratory Tests**

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

\* Assess for acute HIV infection (see Figure 4)

# Rationale for lipid measurement with TAF/FTC

In the DISCOVER trial of TAF/FTC versus TDF/FTC for PrEP among MSM and transgender women:

- Change in weight at 48 weeks was
  - **-0.1 kg** with TDF/FTC
  - **+1.1 kg** with TAF/FTC

}  $p < 0.0001$
- Change in fasting LDL cholesterol at 48 weeks was
  - **+1 mg/dL** with TAF/FTC
  - **-7 mg/dL** with TDF/FTC

}  $p < 0.001$
- Change in fasting triglycerides at 48 weeks was
  - **+4 mg/dL** with TAF/FTC
  - **0 mg/dL** with TDF/FTC

}  $p < 0.002$

**Table 7 Timing of CAB PrEP-associated Laboratory Tests**

| 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                |               |           | MSM^/TGW~ only | Heterosexually active women and men only | X  | MSM/TGW only      |
| Gonorrhea | X                |               |           | MSM/TGW only   | Heterosexually active women and men only | X  | MSM/TGW only      |
| Chlamydia | X                |               |           | MSM/TGW only   | MSM/TGW only                             | Heterosexually active women and men only | MSM/TGW only      |

\* HIV-1 RNA assay

X all PrEP patients

^ men who have sex with men

~ persons assigned male sex at birth whose gender identification is female

**Why no assessment for viral hepatitis in those at risk?**

# HIV RNA assays for monitoring those with antiretroviral exposure

## Rationale:

- Antiretrovirals impact HIV test performance
- Antigen/antibody positivity may be delayed beyond that of an HIV RNA assay for incident infections by a mean of
  - 98 days in those receiving CAB-LA
  - 31 days in those receiving TDF/FTC

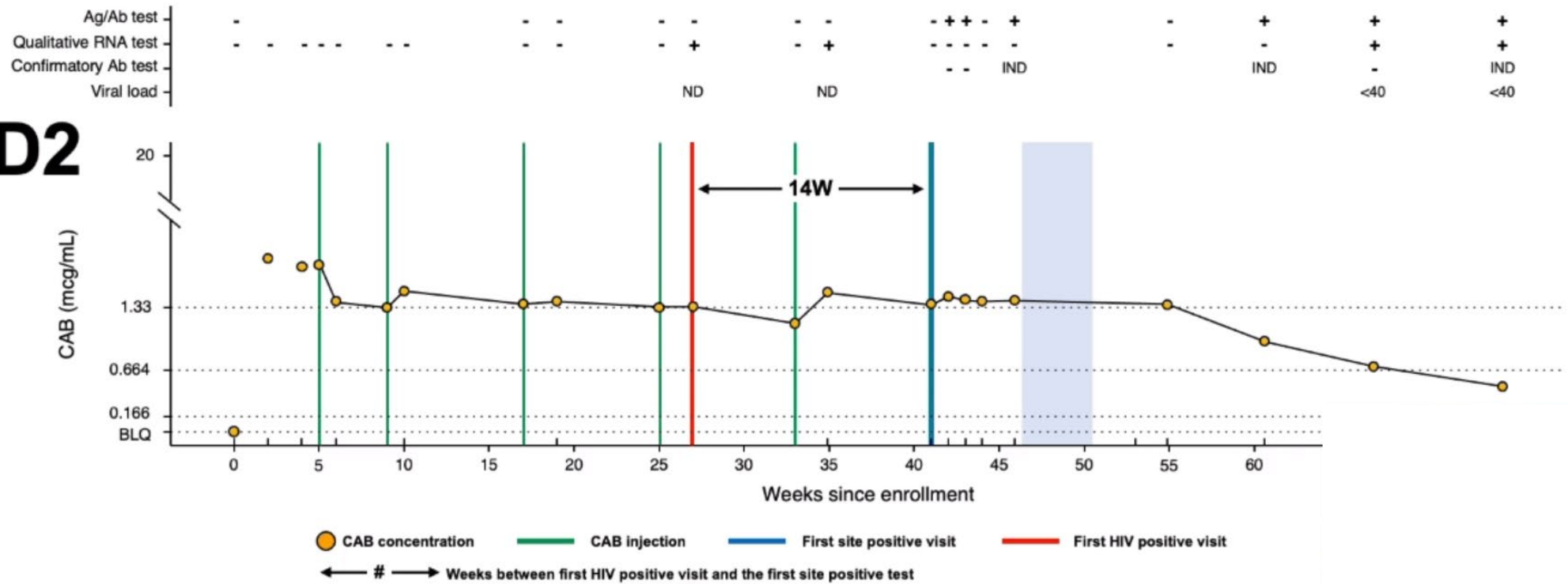
## Questions and challenges:

- Is this necessary for oral PrEP?
- Obtaining HIV RNA assays for people who are un- or underinsured
- Limitations of the USPSTF/ACA provision



# An example of delayed seroconversion with CAB-LA

**D2**



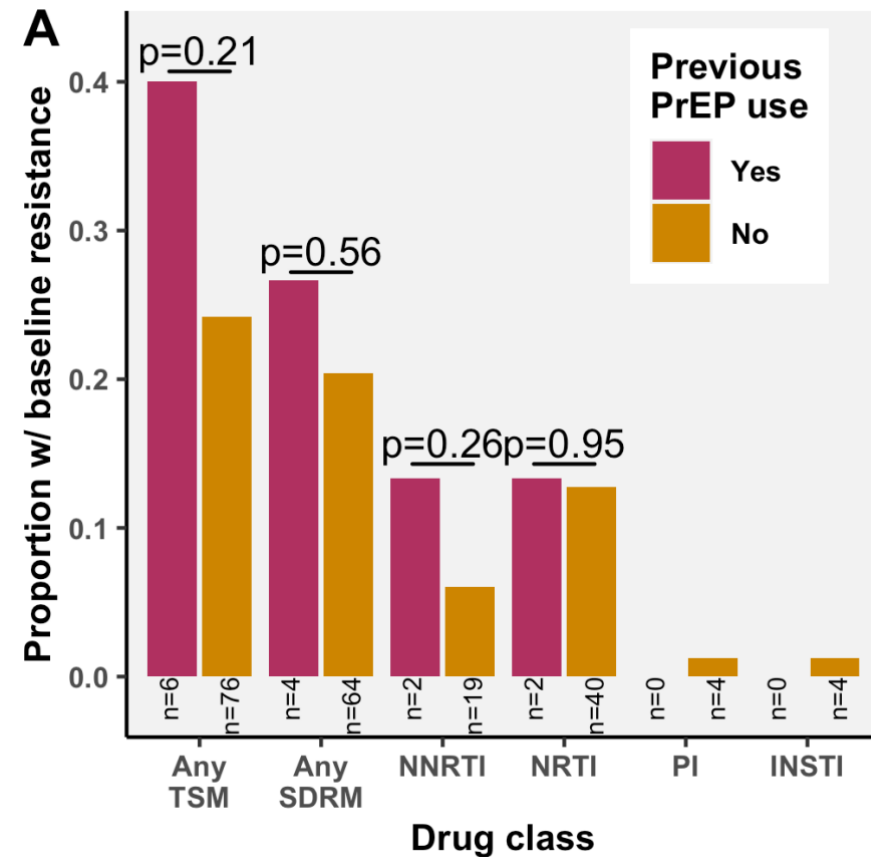
The shaded area represents time on ART.

# HIV RNA assays for those receiving CAB-LA for PrEP

- Low viral load INSTI genotypes for people who acquired HIV despite CAB-LA in HPTN 083
- Among 7 cases, RNA assays would have detected HIV before a major INSTI mutation was detected in 4 cases and before additional major INSTI mutations in 2 cases
- Authors' conclusions: CAB-LA is still a good option for PrEP even when resources do not permit RNA assays

# HIV drug resistance in people who seroconvert despite oral PrEP is not common.

- Analysis of HIV drug resistance among people in British Columbia, comparing those who had used PrEP versus those who had not
- There was no association between previous PrEP use and HIV drug resistance.





# Case

- 35-year-old man taking TAF/FTC for PrEP returns for routine follow-up; no symptoms
- Forgets doses 1-2 times per month
- HIV antibody/antigen **non-reactive**, HIV RNA **84**

# Poll

In addition to sending additional testing, what would you do now?

- A. Stop TAF/FTC
- B. Start a 3-drug regimen for HIV treatment
- C. Continue TAF/FTC

# Managing ambiguous HIV test results for people taking PrEP

1. Ask about medication adherence since the last test
2. Repeat blood testing for HIV antibody/antigen and HIV RNA after a few days
3. Manage antiretrovirals while repeating testing:

| Strategy                          | Pros   | Cons  |
|-----------------------------------|--|---|
| <b>Continue PrEP</b>              | For adherent patients, ambiguous results are likely false positives; provides ongoing protection against HIV | Risk of HIV drug resistance if truly infected           |
| <b>Add a third antiretroviral</b> | Provides a fully suppressive treatment regimen   | HIV test results may remain ambiguous if truly infected |
| <b>Stop PrEP for 1-2 weeks</b>    | Facilitates clarification of HIV status  | Removes PrEP's protection if HIV-uninfected             |

# Case, continued

Clinical course:

- **Day 3:** Asymptomatic, TAF/FTC stopped, testing repeated, HIV antibody/antigen **non-reactive**, HIV RNA **1,820**
- **Day 9:** Fevers, chills, myalgias, nausea
- **Day 10:** HIV antibody/antigen **reactive**, HIV confirmatory assay **non-reactive**, HIV RNA **4,850,000**; TAF/FTC/BIC started
- **Day 36:** HIV confirmatory assay **reactive**, HIV RNA **153**

An HIV genotype obtained on day 3 ultimately returned without reverse transcriptase mutations.

# Summary

- Inform all sexually active people about the availability of PrEP.
- Choose among TDF/FTC, TAF/FTC, and CAB-LA based on patient preference, cost, comorbidities, and source of HIV risk.
- Consider on-demand PrEP for MSM and same-day PrEP if it is logistically feasible.
- Include HIV RNA assays in monitoring on PrEP, especially for CAB-LA.