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.


Harris NS, MMWR Morb Mortal Wkly Rep, 2019
Proportion of eligible people prescribed PrEP in New England, 2018

Harris NS, MMWR Morb Mortal Wkly Rep, 2019
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
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.

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

- Assess sexual risk for all PWID
- Ever Injected Drugs?
  - Yes
    - Injected past 6 months?
      - Yes
        - Shared injection equipment?
          - Yes
            - Prescribe PrEP
          - No
            - Prescribe if requested
      - No
        - Prescribe if requested
  - No
    - Prescribe if requested
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.

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

Delany-Moretlwe S, Lancet, 2022
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.”

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

Perceptions among 234 people with opioid use disorder in CT

Shrestha R 2020
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.

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))

Delany-Moretlwe S, Lancet, 2022; accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf
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 (e.g., time)
- Standard of care for other medical conditions (e.g., 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

<table>
<thead>
<tr>
<th>Medication</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral TDF/FTC</strong></td>
<td>→ Prevents HIV acquisition through sex and injection drug use</td>
<td>→ Should not be used when estimated creatinine clearance is &lt; 60 mL/min</td>
</tr>
<tr>
<td></td>
<td>→ Effective when used in an on-demand fashion among MSM</td>
<td>→ Risks of renal adverse events and decreased bone mineral density</td>
</tr>
<tr>
<td></td>
<td>→ Available as a generic</td>
<td></td>
</tr>
<tr>
<td><strong>Oral TAF/FTC</strong></td>
<td>→ Prevents HIV acquisition through sex</td>
<td>→ Use in an on-demand fashion or among cisgender women has not been studied</td>
</tr>
<tr>
<td></td>
<td>→ Less likely than TDF/FTC to adversely affect kidneys or bone</td>
<td>→ Risk of weight gain and dyslipidemia</td>
</tr>
<tr>
<td></td>
<td>→ Can be used if the estimated creatinine clearance is ≥ 30 mL/min</td>
<td></td>
</tr>
<tr>
<td><strong>Intramuscular CAB (CAB-LA)</strong></td>
<td>→ Superior to TDF/FTC for PrEP among MSM, transgender women, and cisgender women</td>
<td>→ Requires more frequent clinic visits than oral PrEP</td>
</tr>
<tr>
<td></td>
<td>→ Every-two-month injections obviate the need for taking a pill daily</td>
<td>→ Injection site reactions are common but tend to be mild</td>
</tr>
<tr>
<td></td>
<td></td>
<td>→ Limited data about safety in pregnancy</td>
</tr>
</tbody>
</table>
Laboratory tests NOT routinely recommended for PrEP

DEXA
Liver enzymes
Complete blood counts
Urinalyses
Table 5  Timing of Oral PrEP-associated Laboratory Tests

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

* 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  \( p < 0.001 \)
  - -7 mg/dL with TDF/FTC

- Change in fasting triglycerides at 48 weeks was
  - +4 mg/dL with TAF/FTC  \( p < 0.002 \)
  - 0 mg/dL with TDF/FTC

Mayer KH, Lancet, 2020; Spinner CD, IAS 2019
Why no assessment for viral hepatitis in those at risk?

Table 7  Timing of CAB PrEP-associated Laboratory Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Initiation Visit</th>
<th>1 month visit</th>
<th>Q2 months</th>
<th>Q4 months</th>
<th>Q6 months</th>
<th>Q12 months</th>
<th>When Stopping CAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV*</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Syphilis</td>
<td>X</td>
<td></td>
<td></td>
<td>MSM/TGW only</td>
<td>Heterosexually active women and men only</td>
<td>X</td>
<td>MSM/TGW only</td>
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<tr>
<td>Gonorrhea</td>
<td>X</td>
<td></td>
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* 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
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
  o 98 days in those receiving CAB-LA
  o 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

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

Eshleman S, CROI 2022, Abstract 95
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.

McLaughlin A, CROI 2022, Abstract 839
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:

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