Pre-Exposure Prophylaxis (PrEP) Clinical Quick Reference

Version 7.0 – August 2022

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The information contained in this publication is intended for medical professionals, as a quick reference to the national guidelines. This resource does not replace nor represent the comprehensive nature of the published guidelines. Recognizing the rapid changes that occur in this field, clinicians are encouraged to consult with their local experts or research the literature for the most up-to-date information to assist with individual treatment decisions for their patient. If your patient should experience a serious adverse event, please report the event to the FDA's MedWatch program to help increase patient safety.

If you do not have a local expert on PrEP available to you, the **National Clinician Consultation Center** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more at **https://nccc.ucsf.edu** or call **(855) 448-7737** (Monday through Friday, 9AM-8PM ET).

ABOUT THIS DOCUMENT

Following the release of the December 2021 updates of the USPHS/CDC PrEP clinical practice guideline and clinical providers' supplement, the UNC partner site of the Southeast AIDS Education & Training Center (SE AETC) began to receive requests for assistance in navigating and implementing the changes recommended in the updates.

The purpose of this document is:
1. to condense the most important elements of the CDC guidelines into a shorter reference document,
2. to address some of the questions about the guidelines that arose in conversation with PrEP providers,
3. to provide context around some of the changes CDC made relative to prior editions of the guidelines, and
4. to help providers understand where gaps still exist in the guidelines and offer potential solutions.

Care has been taken to indicate where suggestions deviate from the CDC's official guidelines, with explanation or rationale for those deviations contained in footnotes or bulleted comments. Providers should use their best clinical judgment when making decisions about individual patient management or changes to practice-level procedures.

Acknowledgments

- Thanks to Dr. Dawn Smith at the CDC Division of HIV Prevention for clarification on HIV testing algorithms in the 2021 guideline update, and to Dr. Raphael Landovitz at UCLA for feedback on the alternative HIV testing algorithms contained in this document.
- Thanks to Dr. Mehri McKellar and Dr. Charles Burns at Duke University for their review and comments on a final draft.
- Funding for this resource was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned in this resource are for training and identification purposes onl

Table 1: Suggested Step-by-Step Checklist for Providers Initiating PrEP

T4 indicates detailed info available in Table 4

1 Assess need and review available options

Having ANY of these factors places the individual at risk for acquiring HIV – *but always consider the big picture and individual context*

Risks for sexual transmission (prior 6 mos) *
- ❑ Anal or vaginal sex
- ❑ Any bacterial STI diagnosis †
- ❑ Sex partner(s) w/HIV, regardless of viral load
- ❑ Sex partner(s) with unknown HIV status ‡
- ❑ Any condomless sex

Risks for parenteral transmission
- ❑ Injected any substance(s) in prior 6 months §
- ❑ Shared injection equipment
  - needles & "works" (paraphernalia)
  - *consider anabolic steroids, body fillers, etc.*
- ❑ Injecting partner(s) with HIV

Familiarize patient with PrEP option(s) available to them, based on their sexual behavior and potential risk(s):

Daily oral FTC/TDF Truvada	"On-demand" oral FTC/TDF	Daily oral FTC/TAF Descovy	Every 2m IM CAB-LA Apretude
cisMSM PWID, cisWSM TGWSM, cisMSW TGMSM ¶	cisMSM only #	cisMSM, TGWSM **	cisMSM PWID ††, cisWSM TGWSM, cisMSW TGMSM ¶

2 Determine clinical eligibility

WITHIN 90 DAYS BEFORE starting PrEP, check hepatitis B status and renal function. ‡‡

- ❑ Hepatitis B surface **antigen** (sAg) CDC-REQUIRED FOR ORAL PrEP
- ❑ Hepatitis B surface **antibody** (sAb) CDC-RECOMMENDED FOR ALL
- ❑ Serum creatinine CDC-REQUIRED FOR ORAL PrEP
- ❑ Creatinine clearance (Cockcroft-Gault) CDC-REQ'D FOR ORAL PrEP
- ❑ Urinalysis (to establish baseline) A SUGGESTION FOR ORAL PrEP

CAUTION if active hepatitis B (sAg+)
- FTC, TAF, and TDF treat HBV; use may cause "flare" T4
- For FTC/TDF (Truvada), eCrCl must be ≥ 60 mL/min
  → CANNOT dose-reduce FTC/TDF for PrEP if eCrCl < 60 mL/min
- For FTC/TAF (Descovy), eCrCl must be ≥ 30 mL/min

WITHIN 7 DAYS BEFORE starting PrEP, test for HIV infection. §§ T4

Order ONE of these two options (with or without rapid / PoC testing)
- ❑ **Automated, lab-based Ag/Ab combo assay (4th/5th gen)** ← CDC-PREFERRED
- ❑ Automated, lab-based IgM/IgG-sensitive Ab assay (3rd gen)

- **Rapid testing should ALWAYS be accompanied by a blood draw for formal, lab-based testing**
- NEVER use oral fluid-based rapid testing (e.g., OraQuick ADVANCE) for PrEP initiation or f/u

IF CLIENT/PATIENT HAS HIGH-RISK EXPOSURE(S) WITHIN PRIOR ~14 DAYS AND/OR RECENT ANTIRETROVIRAL USE, OBTAIN AN HIV RNA (quantitative or qualitative) IN ADDITION TO ONE OF THE ASSAYS ABOVE. ¶¶

Any of these sxs in prior 4 weeks? Consider acute HIV.

Fever, Fatigue, Skin rash | Headache, Pharyngitis, Night sweats | Myalgia / arthralgia, Cervical adenopathy, Diarrhea / loose stools

You MUST investigate further if acute HIV is a possibility!
- If ANY symptoms are present, rule out acute HIV by checking HIV RNA (quantitative or qualitative) in addition to a laboratory-based, platform-based Ag/Ab assay.

3 Address other baseline needs

- ❑ **Syphilis testing**
- ❑ **Nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia from ALL exposed anatomical sites**
  - Swab the pharynx and/or rectum, as appropriate. Swab the vagina ("blind" is OK). Screen urethra with urine (cis males & TGW).
- ❑ **Hepatitis C antibody** if age 18-79 and never previously tested OR patient has ongoing risks for HCV acquisition T4
- ❑ **Assess need for immunization against hepatitis A** with vaccination history OR hepatitis A antibody testing (IgG or total Ab)
- ❑ **Assess need for immunization against HPV** – ACIP 2019: all persons up to age 26, shared decision-making for ages 27-45 ##
- ❑ **Serum lipid panel** if prescribing FTC/TAF (Descovy), given possibility of increased triglyceride levels due to TAF use
- ❑ **Baseline weight** if prescribing FTC/TAF (Descovy), given potential for weight gain due to TAF use

4 Counsel patient

"Startup syndrome" with FTC/TDF and FTC/TAF
- Around 1 in 6 patients develop mild headaches, nausea, or flatulence; for almost all, these resolve within 1-2 months

Adherence strategies for oral dosing
- Set an alarm, use a pill box, and keep extra dose(s) handy (in car, at work, etc.)
- For daily oral PrEP, pair pill-taking with routine task – something consistent every day, even on weekends
- For "on-demand" oral FTC/TDF, continue q24h dosing through the day **after** the day after patient's last "sex day" ••
  - e.g., if sex on Sat PM, the day after is Sun (take one pill), and the day **after** the day after is Mon (take one pill)
  - if less than 7d from last dosing day to next "sex day," take ONE pill 2-24h before sex; if more than 7d elapse, it's TWO pills

Anticipatory guidance
- Oral doses can be safely taken 3-4 hours before or 3-4 hours after a regularly scheduled dosing time
- No interactions with alcohol or recreational drugs – but encourage patient to avoid sex under the influence
- No drug interactions with hormones for transgender women or men receiving gender-affirming care
- Injections of cabotegravir (CAB) produce soreness ± "knot," peaking by day 3 and resolving by day 7, for most recipients
- There is a 7d "injection window" for every 8 week CAB injections – can administer 42-63 days after prior dose (i.e., 56 days ± 7)
- CAB is present in body up to 15 months after injection; if injections stopped but still at risk, **must cover w/oral PrEP** for 12 mo

MUST RETEST FOR HIV BEFORE RESTARTING PrEP IF MULTIPLE CONSECUTIVE DOSES MISSED AND EXPOSURE(S) OCCURRED IN GAP ∞

5 Prescribe, monitor, and support

First prescription: Dispense enough for 90d with ZERO refills (i.e., #90 if daily FTC/TDF or FTC/TAF; #30 if on-demand FTC/TDF)
- **Under age 25 on FTC/TDF?** Take **4,000 IU per day of vitamin D3** to mitigate TDF's impact on young adult bone density accrual. ££

Subsequent prescriptions: Dispense QS for 90 days with ZERO refills (#90 for daily use, #30 for on-demand FTC/TDF use)

At EVERY visit (q2-3m)
- ❑ **Repeat HIV testing §§§**
  - **Ag/Ab (± RNA) for oral PrEP**
  - **RNA (± Ag/Ab) for IM CAB-LA**
- ❑ Assess adherence, side effects, risk(s)
- ❑ Screen for STIs as appropriate

At least every other visit (q4-6m)
- ❑ Assess ongoing need for PrEP
- ❑ For oral PrEP, check creatinine and eCrCl if over age 50, baseline eCrCl was < 90 mL/min, or other threats to renal safety exist (e.g., HTN, DM)

At least every 12 months
- ❑ Check HCV serologies for MSM, tgWSM, and PWID
- ❑ For oral PrEP, check Cr and eCrCl
- ❑ For FTC/TAF only, check serum lipids

For footnotes, please see next page →

Footnotes for Table 1

Note: "CDC 2021" refers to the 2021 CDC/USPHS PrEP Guidelines

* The CDC 2014, 2018, and 2021 PrEP guidelines use a 6-month "window" for recency of sexual exposures, but CDC 2021 encourages providers to consider individual contexts and not adhere to these criteria too rigidly.

† CDC 2021 lists gonorrhea, chlamydia, and syphilis diagnoses for men who have sex with men (MSM) and transgender women who have sex with men (TGWSM), with only gonorrhea and syphilis listed for cisgender women who have sex with men (cisWSM) & cisgender men who have sex with women (cisMSW). *In other words, chlamydia is not a risk factor by itself among heterosexuals.*

‡ Inclusion of partners with unknown HIV status is derived from Figure 2 on page 23 of CDC 2021. Tables 1a and 1b in CDC 2021 only mention having an "HIV-positive sexual partner" as a risk, not status-unknown partners.

§ A six-month recall "window" is derived from Figure 3 on page 27 of CDC 2021. Neither Table 1a nor Table 1b in CDC 2021 includes this six-month recall period for determining recency of parenteral exposure risk.

¶ We have no data on the preventive benefit of oral or injectable PrEP for transgender men who have sex with men, but we know that they are at increased risk for HIV acquisition via anal and vaginal sex. The benefits of PrEP are presumed to outweigh potential risks.

\# **"On-demand" or "2-1-1" dosing of FTC/TDF is an off-label use that is NOT approved by the FDA.** Although the clinical trials that provided evidence for "2-1-1" FTC/TDF (IPERGAY and ANRS Prévenir) included transgender women who have sex with men, their numbers were very small. CDC 2021 PrEP guidelines recognize data supporting the off-label use of FTC/TDF in this way, but recommend restricting its use to only cisgender MSM, for whom the data are clear and unambiguous. **FTC/TAF should NOT be used on-demand.**

** In the single study leading to FDA-approval of FTC/TAF for PrEP (DISCOVER; ClinicalTrials.gov NCT02842086), there were only 74 trans women out of 5,387 total participants (1.4% of persons studied). There were 22 HIV infections on study (7 on FTC/TAF, 15 on FTC/TDF), but no trans women acquired HIV during study follow-up.

†† Cabotegravir has not been studied for protection against exposures from injecting substances. CDC 2021 includes cabotegravir as an option for PWID, but as a means of protection against sexual exposures these individuals may have (**not** against parenteral exposures).

‡‡ CDC 2014, 2018, and 2021 guidelines do NOT define a window – a 90-day period is our **suggestion** based on clinical experience. Although patients initiating CAB-based PrEP do not need assessments of hepatitis B serostatus or renal function to safely initiate CAB injections, if they discontinue CAB they may need to switch to oral PrEP to cover CAB's pharmacokinetic "tail." Testing could be deferred until the time of a switch from CAB to oral PrEP, it could be performed at baseline, or it could be done at baseline and at switch.

§§ CDC 2021 includes two figures (4a and 4b) intended to simplify the approach to testing. Many PrEP experts have expressed concern about potential ambiguities and confusion with these figures. See the end of this checklist document for the figures and suggested alternative approaches, based on expert opinion.

¶¶ CDC 2021 recommends checking HIV RNA in addition to laboratory-based Ag/Ab testing for persons reporting an "exposure-prone" event in the prior 4 weeks and who are presenting with signs or symptoms of acute HIV within the prior 4 weeks (Fig 4a). CDC 2021 also recommends ordering both Ag/Ab and HIV RNA for all persons who have taken oral PrEP or PEP in the prior 3 months or who received injectable CAB in the prior 12 months (Fig 4b). Many PrEP experts have expressed concern about this approach. See the end of this document for these figures and suggested alternative approaches, based on expert opinion.

\## The 2019 guidance from the CDC's Advisory Committee on Immunization Practices (ACIP) reinforced a prior recommendation to immunize against HPV for all persons aged 11-26 and provided additional guidance for persons who could benefit from "catch-up" immunization if they wish to receive the vaccine after discussion of risks and benefits with their provider.

•• Before prescribing "on-demand" or "2-1-1" oral FTC/TDF, please review **at least** the "Managing the Gaps in Sex" section from Saberi & Scott's April 2020 paper in the *Journal of General Internal Medicine*, available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7174437/

∞ "Forgiveness" (i.e., how many doses might be missed without losing protective efficacy) has been assessed in clinical studies of FTC/TDF (Truvada). For MSM, protection remained high (96% reduced risk) if 4 doses per week were taken as directed. In the ANRS Prévenir study of "2-1-1" or "on demand" FTC/TDF for MSM, 4 doses per week had comparable protection to daily dosing. **There are no data on minimum protective adherence for FTC/TAF (Descovy). There are insufficient data on dosing "forgiveness" among persons for whom vaginal sex or injection drug use are the principal risks for HIV acquisition.** Generally, most PrEP experts would normalize occasional, sporadic missed doses for such patients, while encouraging strategies to help optimize daily adherence.

ℒℒ Vitamin D3 (or D2) supplementation while on **TDF**-based PrEP is a **strong suggestion** based on our interpretation of two clinical studies, discussion with experts who provide services for adolescents and young adults, and assessment of D3's risk-to-benefit ratio in this context.
– Nanayakkara DD, et al. "Effect of Vitamin D Supplementation on Bone Turnover Markers During HIV Pre-Exposure Prophylaxis Using Tenofovir Disoproxil Fumarate-Emtricitabine in Men Who Have Sex with Men." AIDS Res Hum Retroviruses. 2019 Jul;35(7):608-614. PMID: 30907095.
– Havens PL, et al. "Vitamin D3 Supplementation Increases Spine Bone Mineral Density in Adolescents and Young Adults With Human Immunodeficiency Virus Infection Being Treated With Tenofovir Disoproxil Fumarate: A Randomized, Placebo-Controlled Trial." Clin Infect Dis. 2018 Jan 6;66(2):220-228. PMID: 29020329; PMCID: PMC5848310.

§§§ CDC 2021 recommends obtaining Ag/Ab and HIV RNA testing on all patients receiving maintenance PrEP, regardless of the route of administration (oral or IM). The CDC's rationale was to provide one algorithm for testing that could accommodate the special needs of patients receiving cabotegravir, *for whom HIV RNA testing is clearly needed*. Multiple PrEP experts expressed concern to CDC about applying this approach to patients receiving oral maintenance PrEP, since the standard of care from 2012 to 2021 for such patients was testing with a laboratory platform-based Ag/Ab assay by itself. Specific concerns include: (1) the absence of clear, compelling cohort or observational data demonstrating inadequacy of Ag/Ab screening alone for oral PrEP patients and (2) the significant additional burdens that paired Ag/Ab and RNA screening places on healthcare systems in terms of time, logistical effort, and costs. CDC's rebuttal to those concerns was that observational data would accrue in the years following its 2021 guidelines being issued and additional determinations about this approach could be made at a later date. **At UNC, Ag/Ab and RNA testing is not being routinely done for all patients (i.e., it is not per-protocol at UNC).** Patients receiving "maintenance" PrEP with oral FTC/TDF or FTC/TAF are *generally* still screened with Ag/Ab alone. In selected cases, or for patients in whom there is a concern about PrEP failure or symptoms of possible acute HIV infection, HIV RNA is ordered in addition to Ag/Ab testing.

Table 2: Suggested *Minimum* Follow-up Assessments for Patients on Oral PrEP, by Time on Therapy *

Assessment	At 3 Months	At 6 Months	At 9 Months	At 12 Months
Symptom screen for acute HIV	❑	❑	❑	❑
Ask about side effects †	❑	❑	❑	❑
Ask about adherence	❑	❑	❑	❑
Ask about risk-reduction behaviors	❑	❑	❑	❑
Assess need for continued oral PrEP ‡	❑	❑	❑	❑
HIV Ag/Ab (± HIV RNA) §	❑	❑	❑	❑
Syphilis testing ¶	❑	❑	❑	❑
NAAT(s) for gonorrhea & chlamydia ¶	❑	❑	❑	❑
Hepatitis C antibody #				❑
Urinalysis		❑ "if other threats to renal safety are present"		❑ "if other threats to renal safety are present"
Creatinine and eCrCl calculation		❑ if ≥50 years of age **OR** eCrCl <90 mL/min at baseline		❑ for all patients
Serum lipid panel				❑ if using daily FTC/TAF (Descovy)
Pregnancy testing (if appropriate) °	❑	❑	❑	❑
Prescribe a 90d supply of oral PrEP ∞	❑	❑	❑	❑

* This table is adapted from pages 43-44 of the CDC 2021 PrEP guideline. If a client/patient is continuing on oral PrEP after 12 months, restart schedule (i.e., assessments at month 15 are same as those at month 3).

† **This is our suggestion.** CDC 2021 does not include specific guidance to inquire about side effects of oral PrEP.

‡ **This is our suggestion.** CDC 2021 does not include specific guidance for asking clients about desires for PrEP continuation.

§ CDC 2021 recommends obtaining Ag/Ab and HIV RNA testing on all patients receiving maintenance PrEP, regardless of the route of administration (oral or IM). The CDC's rationale was to provide one algorithm for testing that could accommodate the special needs of patients receiving cabotegravir, *for whom HIV RNA testing is clearly needed*. Multiple PrEP experts expressed concern to CDC about applying this approach to patients receiving oral maintenance PrEP, since the standard of care from 2012 to 2021 for such patients was testing with a laboratory platform-based Ag/Ab assay by itself. Specific concerns include: (1) the absence of clear, compelling cohort or observational data demonstrating inadequacy of Ag/Ab screening alone for oral PrEP patients and (2) the significant additional burdens that paired Ag/Ab and RNA screening places on healthcare systems in terms of time, logistical effort, and costs. CDC's rebuttal to those concerns was that observational data would accrue in the years following its 2021 guidelines being issued and additional determinations about this approach could be made at a later date. **At UNC, Ag/Ab and RNA testing is not being routinely done for all patients (i.e., it is not per-protocol at UNC).** Patients receiving "maintenance" PrEP with oral FTC/TDF or FTC/TAF are *generally* still screened with Ag/Ab alone. In selected cases, or for patients in whom there is a concern about PrEP failure or symptoms of possible acute HIV infection, HIV RNA is ordered in addition to Ag/Ab testing.

¶ Table 5 of the CDC 2021 guideline (bottom of page 44) recommends screening MSM and TGW every 3 months for bacterial STIs (gonorrhea, chlamydia, and syphilis), but other populations less frequently (every 6 months). In lieu of rigidly following this schedule, we suggest that PrEP providers: (1) always consider individual client/patient history and contexts before deciding whether to screen at a visit; (2) consistently screen all exposed anatomical sites; and (3) err to the side of more screening, not less screening.

CDC 2021 recommends annual hepatitis C antibody ("serology") only for MSM, transgender women, and persons who inject drugs. For some clients/patients who have greater risks of HCV acquisition (e.g., sharing of needles or "works" for injecting any substance, or sex under the influence of drugs, sometimes called "chemsex"), it may be appropriate to screen more often – or to consider HCV RNA testing in addition to HCV antibody testing. Always consider individual contexts.

° **This is our suggestion.** CDC 2021 is silent on pregnancy testing as a routine part of PrEP service delivery.

∞ For clients/patients using oral PrEP on a daily dosing schedule, the prescription should be for 90 tablets with zero refills.
For those using on-demand or "2-1-1" dosing of FTC/TDF (Truvada), the prescription should be for 30 tablets with zero refills.

Table 3: Suggested *Minimum* Follow-up Assessments for Patients on Cabotegravir, by Time on Therapy *

Assessment	Month 1 (2nd injection)	Month 3 (3rd injection)	Month 5 (4th injection)	Month 7 (5th injection)	Month 9 (6th injection)	Month 11 (7th injection)	Month 13 (8th injection)
Ask about side effects †	❑	❑	❑	❑	❑	❑	❑
Ask about risk-reduction behaviors †	❑	❑	❑	❑	❑	❑	❑
Assess need for cont'd PrEP †	❑	❑	❑	❑	❑	❑	❑
Respond to new questions	❑	❑	❑	❑	❑	❑	❑
HIV RNA and HIV Ag/Ab §	❑	❑	❑	❑	❑	❑	❑
Syphilis testing ¶		❑ MSM & tgWSM	❑ As needed/ on-demand	❑ All clients/ patients	❑ As needed/ on-demand	❑ MSM & tgWSM	❑ MSW & WSM
NAAT(s) for gonorrhea and chlamydia screening ¶		❑ MSM & tgWSM	❑ As needed/ on-demand	❑ All clients/ patients	❑ As needed/ on-demand	❑ MSM & tgWSM	❑ MSW & WSM
Hepatitis C antibody #							❑
Pregnancy testing (if appropriate)°		❑	❑	❑	❑	❑	❑
Administer CAB-LA injection	❑	❑	❑	❑	❑	❑	❑

* This table is adapted from pages 48-52 of the CDC 2021 PrEP guideline. If a client/patient is continuing on every 2 month injectable PrEP after 13 months, restart schedule at month 3 (i.e., **assessments at month 15 are same as those at month 3**).

† **This is our suggestion.** CDC 2021 does not include specific guidance on this issue for clients/patients on CAB-LA injections.

§ Data from the clinical trials that led to long-acting cabotegravir (CAB-LA)'s approval provided clear evidence of delays in "conversion" of antigen-based and antibody-based HIV tests from negative to positive, among study participants who acquired HIV on study and who were randomized to receive CAB. These findings directly informed the CDC 2021 PrEP guideline recommendation to use HIV-1 RNA testing (quantitative or qualitative) as an essential tool to screen CAB-LA recipients for incident HIV infection. Frustratingly, however, CDC 2021 is internally inconsistent as to what HIV testing should be used for clients/patients receiving CAB-LA injections. In Figure 4b (page 31), the recommendation is for plasma specimens (i.e., phlebotomized blood processed in a lab) to be sent for BOTH an antigen/antibody combination assay AND an HIV-1 RNA assay (quantitative or qualitative). Later, in Table 7 (page 50) and on page 52, the recommendation differs: obtain an HIV-1 RNA test and conduct a symptom screening for acute HIV infection. This internal inconsistency contributed to multiple PrEP experts expressing concern about the clarity and usefulness of the 2021 guideline revision. As of 2022, the CDC's HIV diagnostic testing algorithm does NOT allow for HIV RNA to be used *by itself* for HIV diagnostic testing, because of an unacceptably high rate of low-level false-positive results from RNA assays. **At UNC, management of recipients of CAB-LA injections will follow CDC 2021 Figure 4b: sending a phlebotomized specimen for BOTH an HIV antigen/antibody assay AND a quantitative HIV-1 RNA viral load assay at EVERY injection visit.**

¶ CDC 2021 guideline (page 52) recommends screening MSM and TGW every 4 months for bacterial STIs (gonorrhea, chlamydia, and syphilis), but other populations less frequently (every 6 months) while on injectable CAB-LA as PrEP. In lieu of rigidly following this schedule, we suggest that PrEP providers: (1) always consider individual client/patient history and contexts before deciding whether to screen at a visit; (2) consistently screen all exposed anatomical sites; and (3) err to the side of more screening, not less screening.

\# **This is our suggestion.** CDC 2021 is silent on the frequency of hepatitis C screening for clients/patients receiving CAB-LA injections for PrEP. However for oral PrEP, the guidelines recommend annual hepatitis C antibody ("serology") for MSM, transgender women, and persons who inject drugs. For some clients/patients who have greater risks of HCV acquisition (e.g., sharing of needles or "works" for injecting any substance, or sex under the influence of drugs, sometimes called "chemsex"), it may be appropriate to screen more often – or to consider HCV RNA testing in addition to HCV antibody testing. Always consider individual contexts.

° **This is our suggestion.** CDC 2021 is silent on pregnancy testing as a routine part of PrEP service delivery.

Table 4: Notes on Laboratory Tests for Initiating and Managing Patients on PrEP

Test	Notes

HIV antibody testing	• For an overview of HIV testing, see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5718364/
	• **Strong consideration should be given to the use of automated, lab-based antigen/antibody combination assays for ALL PrEP-related HIV testing**. These newer tests are capable of detecting recent infections more reliably than older, IgM/IgG sensitive, "third generation" EIA/ELISA tests. Antigen/antibody combination tests on serum or plasma can identify the presence of viral antigens *before* anti-HIV antibodies develop, narrowing the "window" period of early infection.
	Point-of-care (rapid) antigen/antibody combination tests are NOT as sensitive as lab-based, automated Ag/Ab tests. Unfortunately, the initial version of the only FDA-approved rapid 4th gen (Alere Determine HIV-1/2 Ag/Ab Combo) had exceptionally poor sensitivity in detecting p24 antigen in post-marketing field studies, so it **cannot** be relied upon to exclude acute infection. (For a review, see: http://www.ncbi.nlm.nih.gov/pubmed/26558545). The manufacturer revised this assay, but as of May 2020, its performance from prospectively collected samples has yet to be reported; see https://www.ncbi.nlm.nih.gov/pubmed/27272704 & https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7125248 .
	If any concern exists that a patient may have acute (seronegative) HIV infection, order HIV RNA (viral load) in addition to a 4th generation assay.
	• To order a lab-based, automated 4th generation Ag/Ab combo assay:
	  ○ Quest Diagnostics
	  ▪ Test code 91431, CPT code 87389
	  ▪ "HIV 1/2 Antigen and Antibodies, Fourth Generation, with Reflexes"
	  ○ LabCorp
	  ▪ Test number 083935, CPT code 87389
	  ▪ "HIV p24 Antigen/Antibody with to Confirmation"
	• An IgG-sensitive ("2nd generation") point-of-care (rapid) test may be considered **ONLY IF** fingerstick blood is used as the specimen – NOT oral fluid. Antibody concentrations are much lower in oral transudate than in blood, so the "window" period for antibody detection in oral fluid is longer than in fingerstick blood. For an overview of HIV testing, see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5718364/ .

Serum creatinine	• Estimated creatinine clearance (eCrCl) must be ≥ 60 mL/min to receive FTC/TDF (Truvada)-based PrEP, and ≥ 30 mL/min to receive FTC/TAF (Descovy)-based PrEP. • **Patients with impaired renal function should not be prescribed FTC/TDF (Truvada).** Dose adjustment of FTC/TDF has NOT been studied in the context of PrEP and is ABSOLUTELY NOT recommended in HIV-uninfected patients.

Hepatitis serologies	• Baseline serologies should include AT LEAST the following:
	  ○ Hepatitis B surface antigen (HBsAg) to rule out active, chronic HBV infection
	  ○ Hepatitis B surface antibody (anti-HBs) to assess for the need for immunization
	• Since FTC, TAF, and TDF each have anti-HBV activity, concern exists for the possibility of HBV "flares" among individuals with chronic, replicative HBV who are prescribed PrEP. Data from the iPrEx study showed no evidence of flares, however only 12 of 2499 participants had chronic HBV and only 6 were randomized to receive FTC/TDF. (See: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4752387/). Patients with chronic HBV should be referred for specialty care (ID or hepatology) – which might include TDF, TAF, and/or FTC.
	• Hepatitis C antibody (anti-HCV) testing is encouraged for all patients, however the best evidence supporting this recommendation applies to individuals:
	  ○ aged 18-79 years old (see USPSTF updated recommendation issued 2 March 2020)
	  ○ who have ever injected drugs (with or without shared equipment)
	  ○ who have ever snorted drugs (implements are often shared)
	  ○ having sex of any kind that results in visible mucosal or tissue bleeding
	  ○ engaging in anal sex practices that could produce bleeding or tears in tissue (e.g., sex toys, fisting, rough sex, group sex, or sex under the influence of alcohol or drugs)

Urinalysis with dipstick	• Establishes a baseline so that if any tenofovir-associated renal issues develop, you have a reference point
Syphilis testing	• If not already done in the prior year
NAA tests for gonorrhea & chlamydia	• If not already done in the prior year • Include pharyngeal testing for gonorrhea (± chlamydia) if the patient reports performing oral sex • Include rectal testing for gonorrhea and chlamydia if the patient reports receptive anal sex

Table 5: ICD-10 Diagnostic Codes for PrEP-Related Visits *

Description	Code	Baseline	Follow-Up
Encounter for screening for HIV	Z11.4	❑	❑
Encounter for screening for infections with a predominantly sexual mode of transmission (i.e., screening for STIs)	Z11.3	❑	❑
Counseling related to patient's sexual behavior and orientation	Z70.1	❑	❑
High-risk sexual behavior †	Z72.5	❑	❑
Contact with and (suspected) exposure to HIV	Z20.6	❑	❑
Other long-term (current) drug therapy	Z79.899		❑

* Excerpted from CDC/USPHS PrEP Guidelines, 2014

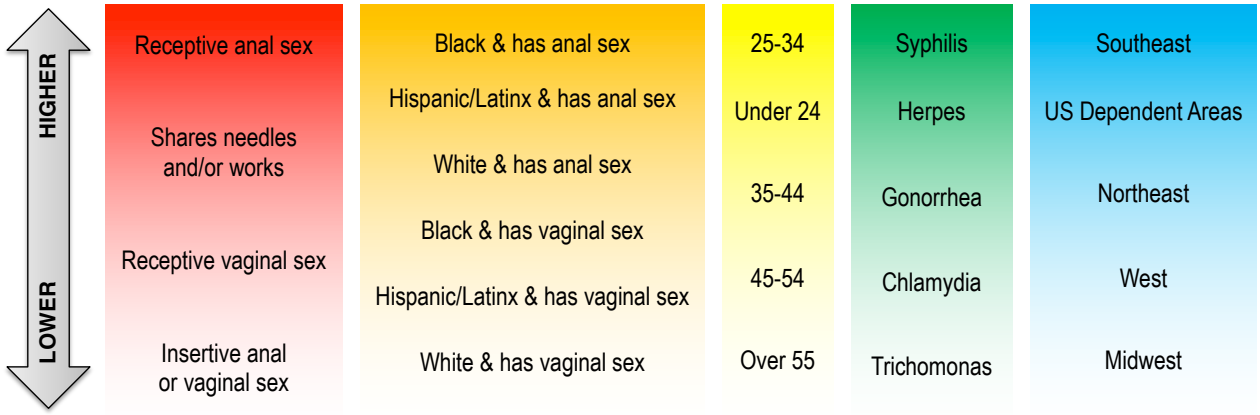
† If you use this ICD-10 code, it may appear on after visit summaries or patient-facing documents. **Strongly consider** letting your patient know in advance that this is not a judgment you're making, it's just one of the diagnostic codes that is necessary to use in order to make sure that PrEP is covered by their insurer.

Table 6: Highly Recommended Resources

Name	Description
PrEP Coverage Brief (NASTAD) https://nastad.org/sites/default/files/2021-11/PDF-NASTAD-PrEP-Coverage-Brief.pdf	Overview of federal regulatory changes in 2021 that reduce out-of-pocket PrEP costs
Paying for PrEP (CDC) https://www.cdc.gov/hiv/basics/prep/paying-for-prep/index.html	Interactive webpage to navigate options for covering the cost of PrEP services
Ready, Set, PrEP (US-DHHS) https://readysetprep.hiv.gov/	Enrollment website for federal program that provides free medication to qualifying persons
Resources for Covering the Costs of PrEP and PEP (PleasePrEPme.org) https://www.pleaseprepme.org/payment	Additional resources to assist uninsured and underinsured patients in covering the cost of PrEP
PrEP Locator (Emory University) https://preplocator.org/	Map-based tool to find PrEP providers listed in the CDC National Prevention Information Network

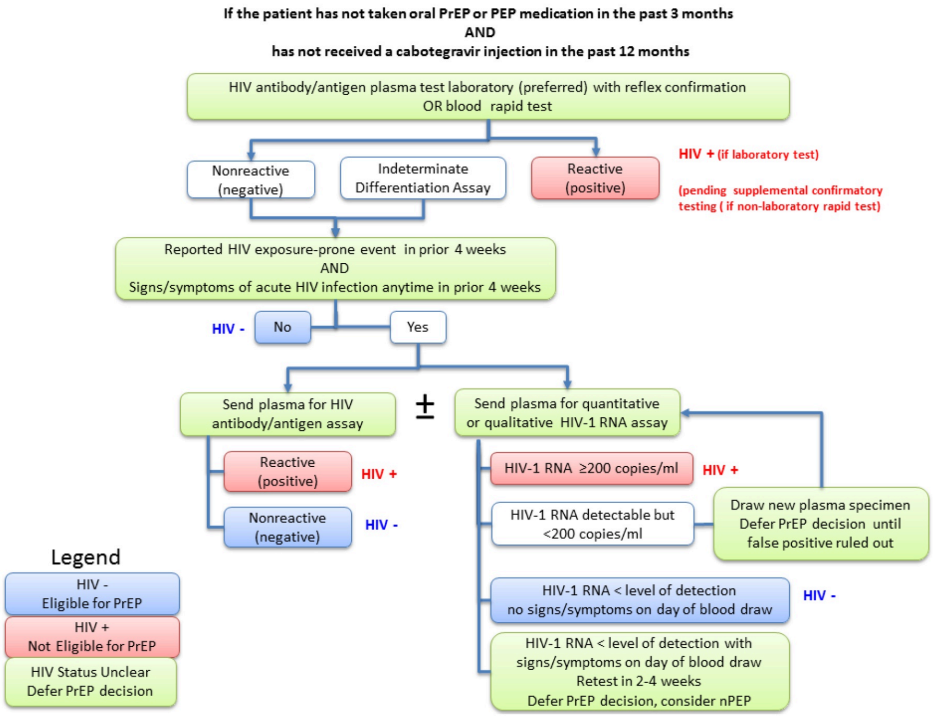
Assessing Risk of HIV Acquisition by Client-Level Characteristics

Adapted from data presented on: https://www.cdc.gov/hiv/statistics/overview/ataglance.html



HIV Testing for Patients/Clients WITHOUT Exposure to Antiretroviral Medications

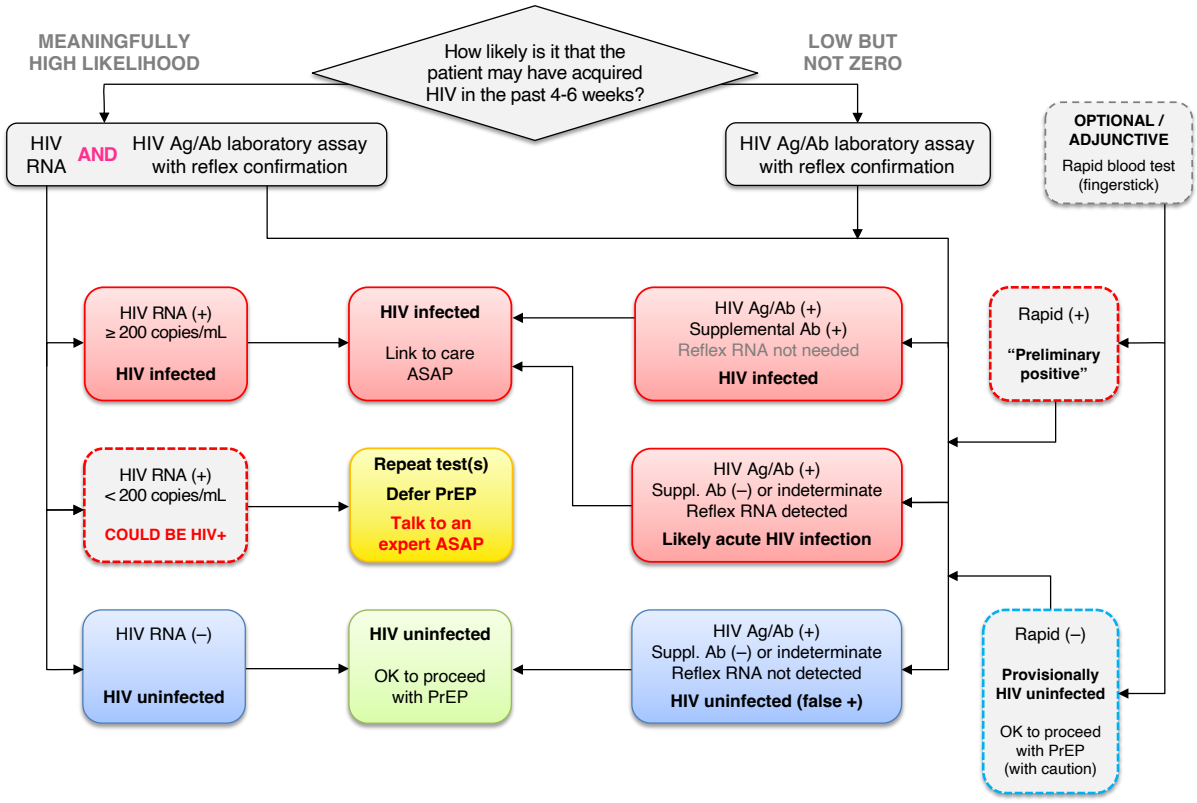
Figure 4a Clinician Determination of HIV Status for PrEP Provision to Persons without Recent Antiretroviral Prophylaxis Use



This diagram is copied directly from the 2021 CDC PrEP Guidelines. PrEP experts have identified ambiguities and "problems" with this diagram, including:

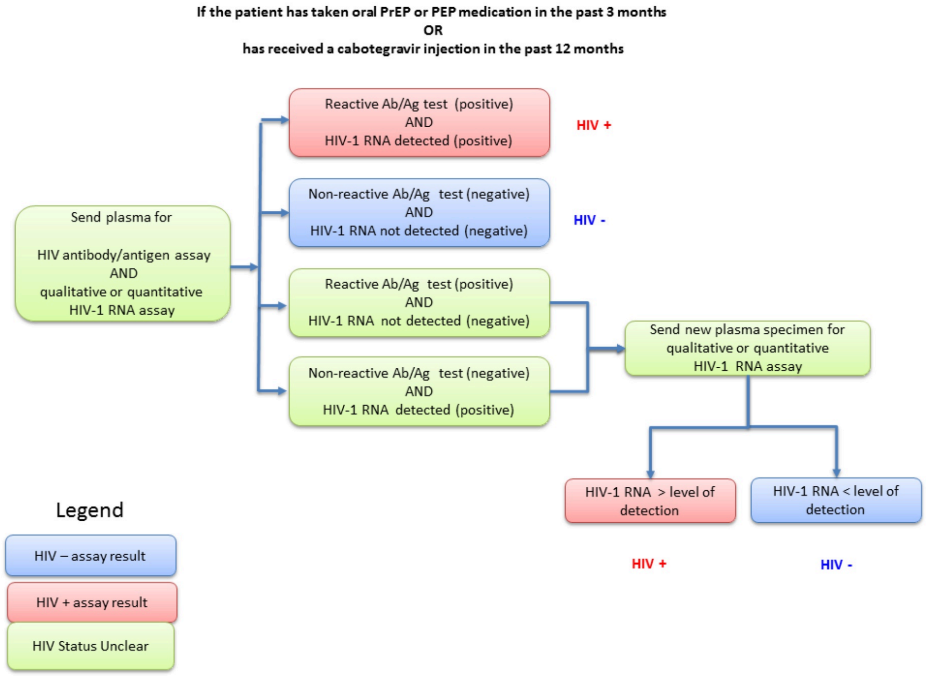
- *First three rows: Asking about exposures and signs/symptoms AFTER ordering an HIV Ag/Ab test is counterintuitive. Generally, obtaining this history from a client/patient helps to determine what type(s) of HIV test would be most informative. Asking about these things AFTER ordering an Ag/Ab assay and getting its result back is confusing.*
- *Second row: The differentiation assay is the second step of a laboratory-based HIV testing algorithm – not the final step. If there is discordance between the Ag/Ab (screening) assay and the differentiation assay, an HIV RNA test is performed to "arbitrate." The "correct" response to an indeterminate differentiation assay result is to wait for the final outcome from lab testing, rather than pursue additional testing before the first round is finalized.*
- *Third row: Many PrEP and sexual health providers use a history of having a recent exposure OR having signs or symptoms of acute HIV as a sufficient "trigger" for obtaining HIV RNA testing in addition to Ag/Ab testing. It's not clear why CDC chose to "require" both (i.e., exposure "AND" sxs)*
- *Fifth row: CDC does not provide guidance regarding the circumstances in which an HIV RNA assay should be used in conjunction with an Ag/Ab assay.*

SUGGESTED ALTERNATIVE – Based on Expert Opinion



HIV Testing for Patients/Clients WITH Exposure to Antiretroviral Medications

Figure 4b Clinician Determination of HIV Status for PrEP Provision to Persons with Recent or Ongoing Antiretroviral Prophylaxis Use



This diagram is copied directly from the 2021 CDC PrEP Guidelines. PrEP experts have identified ambiguities and "problems" with this diagram, including:

- *Preamble: Use of PrEP or PEP in the prior 3 months aligns with the existing schedule for PrEP follow-up, but it doesn't necessarily make sense virologically. That is, use of PEP that ended more than a month ago is unlikely to impact Ag/Ab or RNA currently.*
- *Preamble: Data from the HIV Prevention Trials (HPTN) Study 077 showed that the **median** wash-out period for injectable cabotegravir (CAB) is 10 months for persons assigned male at birth and 15.5 months for persons assigned female at birth – so the 12-month window for recency of CAB exposure is likely too short.*
- *Third row, middle column: If a lab-based Ag/Ab test is reactive, the next step is an antibody-based, supplemental confirmatory test (HIV-1/2 antibody differentiation assay). In this diagram, the results of supplemental tests are not depicted. If the differentiation assay is reactive, then the result of lab-based testing will be reported as "reactive," indicating the patient has confirmed HIV infection. If the differentiation assay is non-reactive, then the discordance between the Ag/Ab assay and differentiation assay results is "arbitrated" using HIV RNA testing. It is very unlikely a clinician would receive a report indicating the results of Ag/Ab testing and RNA testing without the result of the supplemental test, as well.*

SUGGESTED ALTERNATIVE – Based on Expert Opinion