



# CLINICAL GUIDELINES PROGRAM

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

## PrEP to Prevent HIV and Promote Sexual Health

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# PrEP to Prevent HIV and Promote Sexual Health

## Purpose of This Guideline

Pre-exposure prophylaxis (PrEP) is a cornerstone of HIV prevention and is strongly endorsed by New York State (NYS). However, it is underutilized, particularly by communities disproportionately affected by HIV.

**Ending the AIDS epidemic in NYS:** Implemented in April 2015, the *NYS Blueprint to End the AIDS Epidemic by 2020* presents recommended strategies from the Ending the Epidemic Task Force to achieve the first ever decrease in HIV prevalence and end the AIDS epidemic in New York State by the end of 2020. Toward that end, the 3-point plan calls for:

- Identifying individuals with undiagnosed HIV.
- Linking and retaining them in care that includes fully suppressive antiretroviral therapy.
- Facilitating access to PrEP as a proven strategy to prevent HIV acquisition among individuals at high risk.

Including access to PrEP as a pillar of this initiative emphasizes the safety and effectiveness of PrEP as a method to prevent HIV infection. The purpose of this guideline is to provide clinicians throughout NYS with the recommendations needed to successfully start and continue patients on PrEP.

**PrEP efficacy:** Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg in a fixed-dose tablet (TDF/FTC; brand name Truvada) is approved by the U.S. Food and Drug Administration (FDA) for use as PrEP, as part of a comprehensive HIV prevention strategy for individuals at high risk. Multiple randomized, placebo-controlled trials have demonstrated the efficacy of TDF/FTC as PrEP for prevention of HIV infection in all populations. In one study, tenofovir alafenamide 25 mg/emtricitabine 200 mg in a fixed-dose tablet (TAF/FTC; brand name Descovy) was found to be non-inferior to TDF/FTC in a study of, primarily, men who have sex with men and a much smaller number of transgender women [FDA 2019a; Hare, et al. 2019]. Based on those results, it was approved by the FDA on October 3, 2019, for prevention of sexual exposure to HIV in those groups, but not for exposure through receptive vaginal sex, pending further data.

NYS strongly endorses PrEP as an effective, evidence-based biomedical intervention that is a pillar of primary prevention for individuals at high risk of HIV acquisition, emphasizing the importance of prescribing PrEP in conjunction with counseling on safer sex and safer injection practices.

**PrEP uptake:** Although new HIV infections and new HIV diagnoses have steadily declined in NYS, these decreases have not been uniformly realized across all groups. Men who have sex with men (MSM) and communities of color, particularly young MSM and women of color, continue to be overrepresented among people newly infected and diagnosed with HIV [NYSDOH]. Computer simulation modeling suggests that increased PrEP uptake among people in NYS will be the single largest contributor to further reductions in new HIV infections and key to ending the HIV epidemic in NYS [NYSDOH]. However, data indicate that communities of color, women, and individuals accessing Medicaid, 3 groups overrepresented among people with HIV, are accessing PrEP at lower levels than other groups in whom the disease burden is high [ETE Dashboard 2019]. For example, in 2017, 21% of new HIV diagnoses in NYS were in women, but just 8.4% (2,039) of all individuals who accessed PrEP in NYS were women. Nationally, although white MSM account for 30% of new HIV infections, nearly 75% of prescriptions for PrEP in the United States have gone to white MSM, illustrating the need to improve outreach to other communities impacted by HIV [Goedel, et al. 2018; Goldstein, et al. 2018; Jenness, et al. 2019].

**Barriers to PrEP access and use:** The NYS Department of Health (DOH) AIDS Institute (AI) recognizes that a comprehensive approach is necessary to ensure that patients who will most benefit from the use of PrEP have access to it and that their care is managed effectively on PrEP. Awareness and acceptance of PrEP are suboptimal among a broad range of care providers and in communities at risk [King, et al. 2014; Bien, et al. 2017; Blackstock, et al. 2017; Bazzi, et al. 2018; Mayer, et al. 2018; Rael, et al. 2018]. Additionally, retention of individuals in PrEP programs has been a challenge due to both individual and structural barriers to care [Chan, et al. 2016; Serota, et al. 2019]. Populations at the highest risk of acquiring HIV should be prioritized for PrEP outreach and access to ensure that they are aware of PrEP and its benefits. Stigma is important to address because it can keep people who would benefit from PrEP from using it. Actions must be taken to

reduce disparities in access to PrEP among MSM of color, transgender women, black women, and people who inject drugs [King, et al. 2014; Philbin, et al. 2016; Sevelius, et al. 2016; Lancki, et al. 2017; Page, et al. 2017; Biello, et al. 2018; CDC 2018; Garnett, et al. 2018; Morgan, et al. 2018; Sullivan, et al. 2018]. Emerging evidence suggests that transgender MSM are also at higher risk for HIV acquisition [Schein, et al. 2017; Pitasi, et al. 2019] and are a population for whom PrEP outreach and access are needed. This guideline update addresses some structural barriers to PrEP care by advocating for individualization and flexibility in care-delivery models, including monitoring schedules and dosing options.

It is also crucial to address barriers and expand access to PrEP by increasing the number of medical care providers who are aware of and willing to prescribe PrEP. Care providers should also examine any unconscious biases that may influence their willingness to offer PrEP to patients [Calabrese, et al. 2014; Edelman, et al. 2017; Calabrese, et al. 2018]. Clinicians should avoid assumptions about sexual practices and develop comfort and facility in obtaining [routine sexual histories](#) and asking about injection drug use practices to identify potential PrEP candidates among their patients. If a patient asks for PrEP, and it is not medically contraindicated, the patient should be offered a prescription and appropriate follow-up.

- See NYSDOH AI [PrEP Implementation](#) for more information.

In June 2019, the U.S. Preventive Services Task Force (USPSTF) published a [recommendation statement](#) and an [evidence summary](#), which are aligned with the NYS [Ending the AIDS Epidemic Initiative](#). The USPSTF Grade A recommendation states that clinicians should offer “pre-exposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at increased risk of HIV acquisition.” This federal recommendation recognizes PrEP as a preventive service to be covered under the Affordable Care Act, a significant step toward increasing access to PrEP, and further affirms PrEP as a highly effective HIV prevention strategy that clinicians can and should provide to their patients.

In July 2019, the NYS Department of Financial Services Issued a [Circular Letter](#) instructing NYS insurers to cover PrEP without cost-sharing, including co-pays and deductibles, which have been a major financial barrier for many consumers.

#### → KEY POINTS

- In NYS, PrEP is a central component of the standard of care for HIV prevention in those at increased risk.
- Components of primary HIV prevention include PrEP, along with safer sex and safer injection practices.
- Some communities at risk have disproportionate barriers to accessing and using PrEP.
- Medical care provider awareness of and willingness to prescribe PrEP to all patients at risk, regardless of identity, sexual practices, willingness to use condoms, or willingness to cease injection drug use will help reduce some barriers to access and increase uptake of PrEP.
- The NYSDOH [Clinical Education Initiative \(CEI\)](#) and the NYSDOH AI [HIV Education and Training Program](#) offer training in methods of motivational counseling and in prevention interventions.

#### SELECTED RESOURCES: NYSDOH

- |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• <a href="#">Ending the AIDS Epidemic in NYS</a></li> <li>• <a href="#">NYSDOH AI Provider Directory</a></li> <li>• <a href="#">PrEP-Assistance Program Participating Providers</a></li> <li>• <a href="#">PrEP Patient Assistance Program</a></li> </ul> | <ul style="list-style-type: none"> <li>• <a href="#">Payment Options for PrEP</a></li> <li>• <a href="#">Educational Materials for Consumers</a></li> <li>• <a href="#">prepforsex.org</a></li> <li>• <a href="#">NYSDOH FAQs About PrEP</a></li> </ul> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Guideline development:** This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care throughout NYS for people who have HIV, hepatitis C virus, or sexually transmitted infections; people with substance use issues; and members of the LGBTQ community. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the [Medical Care Criteria Committee](#) with developing evidence-based clinical recommendations for use of PrEP to prevent acquisition of HIV infection among people at risk. The resulting recommendations are based on an extensive review of the medical literature and reflect consensus among this panel of experts. Each recommendation is rated for strength and for quality of the evidence (see below). If recommendations are based on expert opinion, the rationale for the opinion is included.

**NYSDOH AI Clinical Guidelines Program Ratings Scheme, Updated June 26, 2019 [a]**

**Strength of Recommendation Ratings**

- A Strong recommendation
- B Moderate recommendation
- C Optional

**Quality of Supporting Evidence Ratings**

- 1 Indicates that the evidence supporting a recommendation is derived from published results of at least one randomized trial with clinical outcomes or validated laboratory endpoints.
- \* Indicates that the evidence supporting a recommendation is strong because it is based on a self-evident conclusion(s) or conclusive, published in vitro data, or because the recommendation articulates well-established, accepted practice that cannot be tested because ethics would preclude a clinical trial.
- 2 Indicates that the evidence supporting a recommendation is derived from published results of at least one well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
- 2† Indicates that the evidence supporting a recommendation has been extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline. When this rating is assigned to a recommendation, the source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text.
- 3 Indicates that a recommendation is based on the expert opinion of the committee members. The rationale for the recommendation is provided in the guideline text.

a. With the June 2019 update, the ratings for quality of supporting evidence were expanded to add the \* rating and the 2† rating.

## PrEP Efficacy

HIV prevention with pre-exposure prophylaxis (PrEP) is the use of antiretroviral medications by individuals who do not have HIV to reduce their risk of acquiring HIV. Daily use of tenofovir disoproxil fumarate (TDF) alone, the combination of TDF/emtricitabine (TDF/FTC; brand name Truvada), and the combination of tenofovir alafenamide/FTC (TAF/FTC; brand name Descovy) have been studied as and proven effective as PrEP in randomized controlled and open-label trials in the following populations:

- Men who have sex with men (MSM): TDF/FTC, TAF/FTC [Grant RM, et al. 2010; McCormack, et al. 2016; Hare, et al. 2019],
- Heterosexual serodiscordant couples: TDF, TDF/FTC [Baeten, et al. 2012],
- Heterosexual men and women: TDF, TDF/FTC [Thigpen, et al. 2012; Van Damme, et al. 2012; Murrain, et al. 2015],
- Transgender women: TDF/FTC, TAF/FTC [Grant RM, et al. 2014; Hare, et al. 2019], and
- People who inject drugs: TDF [Choopanya, et al. 2013].

Efficacy has also been studied and proven effective for event-driven, or “on-demand,” dosing of TDF/FTC as PrEP (taken before and after sexual exposure as opposed to standard daily dosing) for MSM [Molina, et al. 2015; Molina, et al. 2018a].

TDF alone has been effective as PrEP in some populations [Choopanya, et al. 2013; Baeten, et al. 2014], and TAF/FTC is effective in MSM and is likely effective in transgender women [Hare, et al. 2019]; however, to date, only TDF/FTC is effective in preventing HIV infection across all populations, with the greatest effect observed in studies in which high adherence rates were reported [Fonner, et al. 2016].

**MSM:** Studies have demonstrated that TDF/FTC as PrEP is highly effective in MSM [Grant RM, et al. 2010; Grant RM, et al. 2014; Molina, et al. 2015; McCormack, et al. 2016; Hare, et al. 2019]. Although initial data from the iPrEx trial demonstrated only a 44% reduction in rate of HIV acquisition, there was a 92% reduction in sexual transmission when tenofovir was detectable in the blood. No seroconversions occurred in individuals with therapeutic plasma concentrations

of TDF/FTC [Grant RM, et al. 2010]. In the PROUD study [McCormack, et al. 2016], completed after iPrEx, PrEP had an overall efficacy rate of 86% and there were no HIV infections in participants taking TDF/FTC as prescribed. The DISCOVER study [Hare, et al. 2019] showed both TDF/FTC and TAF/FTC to be highly effective in reducing the risk of HIV infection in MSM, with a combined total of 22 new HIV infections in 8,756 person-years of follow-up; all except 2 were either infected at baseline or had low tenofovir plasma concentrations at the time of infection.

**Heterosexual men and women:** Studies have demonstrated TDF/FTC as PrEP to be effective for women and for heterosexual men. In the Partners PrEP study, there was a 67% overall reduction in HIV acquisition in men and women and a 90% reduction in those with detectable drug in blood. [Baeten, et al. 2012]. In the TDF2 study, there was a 62% overall reduction in HIV acquisition, and there were only 2 seroconversions in participants who had detectable drug [Thigpen, et al. 2012]. However, the FEM-PrEP [Van Damme, et al. 2012] and VOICE [Marrazzo, et al. 2015] trials did not demonstrate a benefit of TDF/FTC as PrEP for heterosexual women, although subsequent analyses found that the lack of effect was associated with poor adherence to the prescribed daily PrEP regimen. TAF/FTC has not been studied in cisgender women.

**Transgender women:** In the iPrEx study, TDF/FTC as PrEP was effective in transgender women who adhered to the regimen. In a subanalysis of transgender women in the iPrEx study [Deutsch, et al. 2015], there was no difference in rates of HIV infection between the PrEP and placebo groups; however, none of the transgender women who seroconverted had detectable tenofovir levels, and there were no HIV infections in those who had adequate tenofovir levels. Data indicate that, although tenofovir levels do not affect estrogen levels, the use of estrogen lowers tenofovir levels (area under the curve [AUC], 13%; C24, 17%) [Hiransuthikul, et al. 2018; Cottrell, et al. 2019]. This may contribute to a need for higher adherence among transgender women using estrogens and taking TDF/FTC for PrEP than among other populations, although more research is needed to fully understand the clinical impact of this interaction. TAF/FTC was effective in transgender women [Hare, et al. 2019], but transgender women made up only 1% of the study population.

**Transgender men:** Data are lacking regarding TDF/FTC and TAF/FTC as PrEP for transgender men who have sex with men or with transgender women, despite the increased risk of HIV acquisition in this population [Schein, et al. 2017; Pitasi, et al. 2019]. There are no data as yet on whether testosterone therapy affects tenofovir levels.

**People who inject drugs:** The Bangkok Tenofovir Trial [Choopanya, et al. 2013] is the only randomized controlled trial of PrEP in people who inject drugs. PrEP efficacy with TDF in this study was 49%, although restricting analysis to those with detectable drug in their blood increased efficacy to 74%.

**PrEP failure:** HIV acquisition despite adherence to PrEP is rare. PrEP failure is directly related to suboptimal adherence in all but a small number of cases. In the majority of cases of HIV acquisition despite adherence to PrEP, there was unrecognized HIV infection at initiation. There are case reports of individuals who acquired HIV despite adherence to TDF/FTC as PrEP, measured by tenofovir concentration (hair or dried blood spot samples). These case reports have noted some individuals were exposed to virus resistant to tenofovir and emtricitabine [NYC Health 2016; Knox, et al. 2017], one individual acquired HIV with mutations that should still have conferred sensitivity to TDF/FTC [Cohen SE, et al. 2019], and another acquired wild-type virus while using PrEP [Hoornenborg, et al. 2017b]. It is theorized that in the case of wild-type virus acquisition despite good adherence, exposure to HIV was potentially very high given the number of condomless exposures over the 6-month period and the presence of rectal sexually transmitted infections.

→ KEY POINTS

- TDF/FTC is highly efficacious as PrEP when used as prescribed in all populations.
- TAF/FTC is non-inferior to TDF/FTC as PrEP for sexual exposure in cisgender MSM and transgender women; data are lacking for all other populations.

## TDF/FTC Versus TAF/FTC as PrEP

See *Table 1: TDF/FTC Versus TAF/FTC as PrEP*, below, for a comparison of these 2 PrEP options. TAF/FTC as PrEP was non-inferior to TDF/FTC as PrEP in cisgender MSM and in the small group of transgender women who participated in the DISCOVER trial, a large, double-blinded, active-control study [Hare, et al. 2019]. In that trial, the TAF component was associated with improved biomarkers for renal and bone safety; however, the clinical significance of these changes is unclear, and there was no difference in clinical outcomes regarding adverse events. TAF use was associated with small increases in weight gain and in lipid levels compared with TDF, but the clinical significance of these differences is also not clear.

In a group of volunteers without HIV, TAF had a faster time to effective tenofovir diphosphate concentrations (EC<sub>90</sub>) than TDF (4 hours vs. 3 days) and significantly higher steady state concentrations in peripheral blood mononuclear cells [Spinner, et al. 2019], indicating a potential clinical benefit in terms of time to protection and forgiveness of missed doses, but this is preliminary evidence, and further evaluation is needed.

TAF/FTC has not yet been studied for vaginal exposures in human trials. Study results to date suggest that tenofovir concentrations in vaginal tissue after administration of TAF are lower than for TDF [Garrett, et al. 2016], although TAF does reach high intracellular concentrations in peripheral blood mononuclear cells, and oral TAF/FTC was effective in preventing vaginal SHIV (simian HIV) infections in macaques [Massud, et al. 2018]. Further study of TAF/FTC for protection in vaginal and injection HIV exposures is needed. TAF/FTC has also not been studied in insertive partners in the context of vaginal sex.

TDF/FTC is the preferred regimen for PrEP because of its proven efficacy and safety in clinical trials and its suitability for use as PrEP across all populations. TAF/FTC is an alternative regimen for cisgender MSM and transgender women and is preferred in cisgender MSM and in transgender women who have preexisting renal disease or osteoporosis. TAF/FTC also may be preferable in MSM and transgender women with multiple risk factors for development of either renal disease or osteoporosis. TAF may have an advantage in MSM and transgender female adolescents who have not achieved bone maturation, given favorable bone biomarkers compared with TDF, but this advantage is theoretical, and without clinical data a clear recommendation cannot be made at this time [Hosek, et al. 2017; Hare, et al. 2019; Havens, et al. 2019; Spinelli, et al. 2019].

→ KEY POINTS

- TDF/FTC is the preferred PrEP regimen for all populations.
- TAF/FTC is preferred in the subset of MSM and transgender women who have renal dysfunction or osteoporosis; it may have an advantage in adolescent MSM and transgender women who have not achieved bone maturation.

**Table 1: TDF/FTC Versus TAF/FTC as PrEP**

	TDF/FTC	TAF/FTC
<b>Effectiveness</b>	All populations [Grant RM, et al. 2010; Baeten, et al. 2012; Thigpen, et al. 2012; Van Damme, et al. 2012; Choopanya, et al. 2013; Grant RM, et al. 2014; Marrazzo, et al. 2015; McCormack, et al. 2016; Hare, et al. 2019].	Cisgender MSM and transgender women [a] [Hare, et al. 2019].
<b>Renal safety</b>	<ul style="list-style-type: none"> <li>• Potential effect on renal tubular function. Meta-analysis shows good safety [Pilkington, et al. 2018].</li> <li>• Discontinue if confirmed CrCl &lt;50 mL/min.</li> </ul>	<ul style="list-style-type: none"> <li>• Improved renal biomarkers compared to TDF [Hare, et al. 2019].</li> <li>• Can be used with stage 3 CKD (CrCl 30-59 mL/min).</li> </ul>
<b>Bone safety</b>	Potential decrease in bone mineral density. Meta-analysis shows good safety [Pilkington, et al. 2018].	Favorable bone biomarkers compared with TDF [Hare, et al. 2019].
<b>Weight</b>	Weight neutral.	Mild weight gain observed in studies [Gomez, et al. 2019; Hare, et al. 2019; Hill, et al. 2019; Schafer, et al. 2019].
<b>LDL cholesterol</b>	Small decreases [Orkin, et al. 2018; Hare, et al. 2019].	Small increases [Orkin, et al. 2018; Hare, et al. 2019].
<b>Dosing</b>	Daily dosing is preferred. On-demand dosing is an option in cisgender MSM [Molina, et al. 2015; Molina, et al. 2018b].	Daily dosing only.
<b>Cost</b>	Will go off patent in 2020.	Currently similar to TDF/FTC.

**Abbreviations:** CKD, chronic kidney disease; CrCl, creatinine clearance; FTC, emtricitabine; LDL, low-density lipoprotein; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; TAF, tenofovir alafenamide/emtricitabine; TDF, tenofovir disoproxil fumarate.

a. Transgender women made up only 1% of the DISCOVER study population.

## Risks and Benefits of TDF/FTC and TAF/FTC as PrEP

*Box 1: Benefits and Risks of TDF/FTC and TAF/FTC as PrEP, below, highlights the benefits, risks, and challenges associated with PrEP use.*

Box 1: Benefits and Risks of TDF/FTC and TAF/FTC as PrEP	
Benefits	Risks and Challenges
<ul style="list-style-type: none"> <li>• 99% effective in reducing the risk of HIV acquisition when used as prescribed [CDC 2019].</li> <li>• Regimen is a single tablet taken daily.</li> <li>• TDF/FTC and TAF/FTC have good safety profiles in people who do not have HIV [Tetteh, et al. 2017; Pilkington, et al. 2018; Hare, et al. 2019].</li> <li>• Minimal side effects, most of which resolve fairly quickly or can be managed [Tetteh, et al. 2017; Hare, et al. 2019].</li> <li>• TDF/FTC appears to be safe for use during attempts to conceive and during pregnancy [AIDSinfo 2018] (insufficient safety data for TAF/FTC).</li> <li>• Can decrease anxiety regarding HIV acquisition.</li> <li>• Engages sexually active at-risk individuals in care who are then screened regularly for STIs.</li> </ul>	<ul style="list-style-type: none"> <li>• Safety concerns for individuals with impaired kidney function [FDA 2016].</li> <li>• Uncertainty about time to protection after initiation (see section on <i>Time to Protection</i> in this guideline).</li> <li>• Protection is correlated with adherence to the dosing schedule [Dimitrov, et al. 2016].</li> <li>• No protection against STIs other than HIV.</li> <li>• Compared with TAF, TDF may be associated with reversible decreases in bone density in younger individuals [Havens, et al. 2017].</li> <li>• Continued use after undiagnosed HIV infection may result in development of drug-resistant virus [Lehman, et al. 2015; Hare, et al. 2019].</li> <li>• Requires additional monitoring in patients with chronic hepatitis B virus (see <i>Box 3: Important Clinical Considerations When Prescribing TDF/FTC and TAF/FTC as PrEP</i> in this guideline).</li> <li>• Cost.</li> </ul>
<p><b>Abbreviations:</b> FTC, emtricitabine; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; TAF, tenofovir alafenamide/emtricitabine; TDF, tenofovir disoproxil fumarate.</p>	

## Candidates for PrEP

<input checked="" type="checkbox"/> RECOMMENDATIONS: Candidates for PrEP
<ul style="list-style-type: none"> <li>• Clinicians should recommend pre-exposure prophylaxis (PrEP) for individuals, including adolescents,* who do not have but are at increased risk of acquiring HIV. (A1)</li> <li>• For patients who are completing a course of non-occupational post-exposure prophylaxis (nPEP) and remain at risk for HIV, clinicians should recommend initiation of PrEP immediately after completion of nPEP. (A3) <ul style="list-style-type: none"> <li>◦ See the NYSDOH AI guideline <i>PEP for Non-Occupational Exposure to HIV (nPEP)</i>.</li> </ul> </li> </ul> <p>*The U.S. Food and Drug Administration (FDA) approved the use of tenofovir disoproxil fumarate (TDF/FTC) as PrEP on May 15, 2018. On October 3, 2019, the FDA approved the use of tenofovir alafenamide/emtricitabine (TAF/FTC) as PrEP for cisgender MSM and transgender women, including adolescents, weighing ≥35 kg (~77 lb) at high risk of acquiring HIV.</p>

PrEP should be offered to individuals at increased risk of HIV acquisition, including adolescents, as part of a comprehensive prevention plan (see *Box 2: Individuals Who Should Be Offered Pre-Exposure Prophylaxis*, below). A comprehensive plan includes counseling and education about adherence to PrEP [Liu AY, et al. 2014; Marcus, et al. 2014; Blashill, et al. 2015; Daughtridge, et al. 2015], ongoing monitoring with laboratory tests, education about risk reduction, and discussion of additional HIV prevention options, including use of condoms and safe drug injection practices. Decreased condom use has been observed in some individuals taking PrEP and has been associated with a concomitant rise in other viral and bacterial sexually transmitted infections (STIs) for which PrEP offers no protection; however, this is not a valid reason to withhold PrEP [Liu AY, et al. 2013; Golub 2014; Hojilla, et al. 2016; Kuhns, et al. 2016; Traeger, et al. 2018; Werner, et al. 2018]. (See *STI Screening* in this guideline for more information.)

Patients who remain at increased risk of HIV exposure after completing a course of nPEP and who are negative for HIV at the time of the 4-week test should be offered PrEP, to begin immediately after the last dose of nPEP.

**Box 2: Individuals Who Should Be Offered Pre-Exposure Prophylaxis (PrEP)**

**Candidates who should be offered PrEP include individuals who:**

- Engage in condomless sex with partners whose HIV status is unknown, or who have untreated HIV, or who have unsuppressed virus while on treatment for HIV. [Smith, et al. 2012; Grov, et al. 2013].
- Are attempting to conceive with a partner who has HIV.
- Are at ongoing risk of HIV acquisition during pregnancy through inconsistent condom use with sex partners who have unsuppressed virus [Heffron, et al. 2016].
- Have, or are involved with partners who may have, multiple or anonymous sex partners.
- Engage in sexual activity at parties and other high-risk venues, or have sex partners who do so.
- Are involved, or have partners who may be involved, in transactional sex (i.e., sex for money, drugs, food, or housing), including commercial sex workers and their clients.
- Have been diagnosed with at least 1 bacterial sexually transmitted infection (STI) in the previous 12 months [Zetola, et al. 2009; LaLota, et al. 2011].
- Report recreational use of mood-altering substances during sex, including but not limited to alcohol, methamphetamine [Buchacz, et al. 2005; Zule, et al. 2007; Koblin, et al. 2011; Smith, et al. 2012; Grov, et al. 2013], cocaine, ecstasy, and gamma hydroxybutyrate.
- Report injecting substances or having sex partners who inject substances, including illicit drugs, hormones, or silicone.
- Are receiving non-occupational post-exposure prophylaxis (nPEP) and anticipate ongoing risk or have used multiple courses of nPEP [Heuker, et al. 2012].
- Request the protection of PrEP even if their sex partners have an undetectable HIV viral load (see the discussion of U=U, below).
- Self-identify as being at risk without disclosing specific risk behaviors.
- Acknowledge the possibility of or anticipate engaging in risk behaviors in the near future.

**Do not withhold PrEP from candidates who:**

- Are pregnant or planning a pregnancy.
- Use other risk-reduction practices inconsistently, including condoms.
- Report substance use.
- Have mental health disorders, including those with serious persistent mental illness.
- Report intimate partner violence.
- Have unstable housing or limited social support.
- Report a recent STI.
- Request PrEP even in they have a partner living with HIV with an undetectable viral load.

**PrEP for HIV-serodifferent couples:** For individuals in a serodifferent partnership, PrEP may be useful, even if the partner with HIV is taking suppressive antiretroviral therapy (ART). Data from the Partners in Prevention HSV/HIV Transmission Study [Donnell, et al. 2010] and the HPTN 052 study [Cohen MS, et al. 2011] demonstrated up to a 92% and 96% reduction, respectively, in HIV transmission risk in serodifferent heterosexual couples when the partner with HIV was on suppressive ART. HIV is transmissible if a person’s viral load is not fully suppressed, which may take up to 6 months or longer after ART initiation; once an undetectable viral load is achieved, HIV is not sexually transmissible [Mujugira, et al. 2016].

In the Partners Demonstration Project, use of TDF/FTC as PrEP as a “bridge” was highly effective in protecting the person without HIV during the first 6 months of a partner’s ART [Baeten, et al. 2016]. Subsequently, in the Partner [Rodger AJ, et al. 2016] and Partner 2 [Rodger A, et al. 2018] studies and the Opposites Attract study [Bavinton, et al. 2017], there were zero linked sexual transmissions to an HIV-negative partner when the partner with HIV had an undetectable viral load. In September 2017, the NYSDOH endorsed the *Undetectable = Untransmittable (U=U)* consensus statement from the Prevention Access Campaign [Zucker HA 2017; Prevention Access Campaign 2019]. (See also NYSDOH AI *U=U Guidance for Implementation in Clinical Settings.*)

In a serodifferent partnership, the person who does not have HIV may decide to go on PrEP even if their partner has achieved an undetectable viral load on treatment. Although this supplemental protection is likely not necessary in light of data supporting treatment in preventing HIV transmission, PrEP should be offered along with a clear discussion of U=U. It

is important to note that the partner without HIV may choose to take PrEP for other reasons, including if they have additional sexual partners, are unsure of a sex partner’s viral load or ability to maintain viral suppression, or feel more secure about and in control of their sexual health with the protection of PrEP.

Although the efficacy of TDF/FTC as PrEP during attempts to conceive has not been formally studied, it is an option for individuals who do not have HIV. Evidence suggests that PrEP in this setting does not affect male fertility [Were, et al. 2014] and is safe during the periconception period [Mugo, et al. 2014]. TAF/FTC has not been studied in the context of attempts to conceive.

**PrEP for adolescents:** On May 15, 2018, the FDA approved the use of TDF/FTC as PrEP in adolescents weighing  $\geq 35$  kg (~77 lb.) [FDA 2018]. The Centers for Disease Control and Prevention and the International Antiviral Society–USA previously extended the indication for TDF/FTC to include PrEP for adolescents at increased risk of acquiring HIV [Marrazzo, et al. 2014; CDC 2017]. To date, there is no evidence of increased TDF/FTC toxicity in adolescents taking this combination as part of an ART regimen. TDF/FTC as PrEP was safe and effective in adolescents, with no renal events or bone fractures noted [Hosek, et al. 2017]. Concerns regarding bone loss in younger age groups have been raised, with 2 studies reporting a decline in bone mineral density [Havens, et al. 2017] [Hosek, et al. 2017]. Bone density changes associated with TDF use are reversible on discontinuation in adults [Grant R, et al. 2016] and in young men who have sex with men, aged 18 to 22 years [Hosek, et al. 2017]. Data on bone density recovery after discontinuation of TDF/FTC as PrEP is not available for adolescents younger than 18 years. Studies are in progress to determine safety of the drug for adolescents over longer periods of time. TAF/FTC was approved by the FDA for use as PrEP in adults and adolescents in October 2019. There are no specific data on bone safety in adolescents taking TAF/FTC as PrEP; however, given the more favorable bone biomarkers of TAF versus TDF, TAF may have an advantage in MSM and transgender female adolescents who have not achieved bone maturation, but this advantage is theoretical, and without clinical data a clear recommendation cannot be made at this time. Modeling studies have shown the potential for PrEP to be highly effective at reducing HIV incidence in adolescent MSM communities, through both direct use by adolescents and indirectly by reducing HIV prevalence among their young adult sex partners [Goodreau, et al. 2018; Hamilton, et al. 2019].

→ **KEY POINTS**

- PrEP effectively enhances protection during periods when individuals, including adolescents, are at greatest risk of acquiring HIV.
- In New York State, PrEP is a central component and standard of care for HIV prevention in those at increased risk of acquiring HIV.
- Education about PrEP should stress that it is highly effective but is not 100% protective against HIV acquisition and does not protect against other STIs.
- Duration of PrEP use will depend on the length of time an individual remains at increased risk for HIV (see section on *Discontinuing PrEP* in this guideline for more information).
- The 2-drug PrEP regimens of TDF/FTC and TAF/FTC are not adequate as HIV treatment. If HIV infection is confirmed, PrEP should immediately be converted to a full ART regimen for HIV treatment. (See *Managing a Positive HIV Test Result* in this guideline.)

A 2017 amendment to the New York Codes, Rules and Regulations (NYCRR) grants minors the capacity to consent to PrEP and post-exposure prophylaxis (PEP) without parental/guardian involvement. See the NYSDOH AI *Forum on PrEP for Adolescents: Successes, Challenges & Opportunities* for an extensive discussion of considerations for PrEP in adolescents.

★ **NEW YORK STATE LAW**

- [New York Consolidated Laws, Public Health Law – PBH Article 2305](#) has long established the legal capacity of minors to consent to treatment and preventive services for sexually transmitted diseases (STDs). Provisions in Article 2305 require that the Commissioner of Health promulgate a list of sexually transmitted diseases. A 2017 amendment to Article 2305 added HIV to the list of STDs, thereby bringing minor capacity to consent to HIV treatment and preventive services on par with other STDs. In addition, under Article 2305, medical or billing records may not be released or made available to the parent or guardian without the minor patient’s permission. For more information, see [NYS Register/April 12, 2017: Rule Making Activities](#).

# Clinical Considerations With TDF/FTC or TAF/FTC as PrEP

*Box 3: Important Clinical Considerations With TDF/FTC or TAF/FTC as PrEP, below, discusses the clinical considerations associated with PrEP use.*

## Box 3: Important Clinical Considerations With TDF/FTC or TAF/FTC as PrEP

### ☑ If the patient has active chronic hepatitis B virus (HBV):

- Tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), and emtricitabine (FTC) are active against HBV. For more information, see [AASLD guidelines for treatment of chronic hepatitis B](#).
- TDF and TAF are approved by the U.S. Food and Drug Administration (FDA) for the treatment of HBV. When taken daily, TDF/FTC or TAF/FTC may be used as PrEP and concomitant HBV treatment.\*
- Continuation of TDF, TDF/FTC, TAF, or TAF/FTC as HBV treatment should be recommended for patients who do not have HIV and for whom PrEP is no longer indicated.
- Discontinuation of TDF/FTC or TAF/FTC in patients with chronic HBV requires close monitoring for rebound HBV viremia.
- Individuals with chronic HBV who are not candidates for PrEP should be evaluated for treatment that follows published guidelines [Terrault, et al. 2016]. For more information, see the NYSDOH AI guideline [HBV-HIV Coinfection](#).

### ☑ If the patient is pregnant or attempting to conceive:

- Information about the potential benefits and risks of taking TDF/FTC during pregnancy is an essential component of shared decision-making regarding risk reduction.
- TAF/FTC is not approved for use as PrEP in this population.
- HIV acquisition risk is higher during pregnancy and is at its highest in the late pregnancy and early postpartum periods [Thomson, et al. 2018].
- Risk of perinatal transmission is significantly higher during acute seroconversion when a patient is pregnant or breastfeeding [Singh, et al. 2012; Drake, et al. 2014].
- TDF/FTC as PrEP may be continued during pregnancy and breastfeeding if risk of HIV acquisition is ongoing.
- Suppressive antiretroviral therapy (treatment as prevention) for a partner who has HIV is an important component of risk reduction.
- Prospectively report information regarding use of PrEP during pregnancy to the [Antiretroviral Pregnancy Registry](#).

### ☑ If the patient is an adolescent:

- TDF/FTC (for all populations) and TAF/FTC (for cisgender MSM and transgender women) as PrEP are appropriate for adolescents who are at risk of acquiring HIV and weigh  $\geq 35$  kg (~77 lb).
- A 2017 amendment to the New York Codes, Rules and Regulations (NYCRR), grants minors the capacity to consent to PrEP and PEP without parental/guardian involvement.

### ☑ If the patient is at risk of chronic kidney disease (e.g., age >40 years, hypertension, or diabetes), or has preexisting mild kidney disease with creatinine clearance (CrCl) <60 mL/min:

- The greater possibility of kidney disease among individuals who have risk factors is an essential component of the risk-benefit discussion and shared decision-making regarding initiation of TDF/FTC or TAF/FTC as PrEP.
- More frequent renal monitoring may be required for patients at risk of renal disease or who are older than 40 years who elect to use TDF/FTC or TAF/FTC as PrEP.
- TDF/FTC should not be initiated in individuals who have a CrCl <60 mL/min. TAF/FTC is an option for PrEP in MSM and transgender women with renal disease and a CrCl >30 mL/min.

### ☑ If the patient is taking other medications:

- A thorough medication history that includes over-the-counter medications, such as nonsteroidal anti-inflammatory drugs, may reveal concomitant nephrotoxic drugs and potential need for increased renal monitoring.

**Box 3: Important Clinical Considerations With TDF/FTC or TAF/FTC as PrEP**

**☑ If the patient has osteopenia, osteomalacia, or osteoporosis:**

- The risk of bone loss for individuals who have preexisting risk factors or documented osteopenia, osteomalacia, or osteoporosis is an important component of the risk-benefit discussion and shared decision-making regarding initiation of TDF/FTC as PrEP. TAF/FTC is preferred for cisgender MSM and transgender women with osteoporosis.

\*TDF and TAF are approved by the FDA as treatment for HBV. FTC is also active against HBV but is not FDA-approved for HBV treatment. TDF or TAF in combination with FTC or lamivudine (3TC), which is FDA-approved for HBV treatment and is molecularly similar to FTC, is commonly used in patients with HIV-HBV coinfection as part of an antiretroviral regimen to treat both infections.

## Contraindications to PrEP Initiation

**☑ RECOMMENDATIONS: Contraindications to TDF/FTC and TAF/FTC as PrEP**

- Pre-exposure prophylaxis (PrEP) is contraindicated in any individual with HIV; clinicians should not prescribe either tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide/emtricitabine (TAF/FTC) as PrEP for any person who has a documented HIV diagnosis; in such cases, a full therapeutic antiretroviral regimen is required. (A1)
  - See NYSDOH AI guideline *Selecting an Initial ART Regimen*.
- Clinicians should not prescribe TDF/FTC as PrEP for any individual with a confirmed creatinine clearance (CrCl) <60 mL/min; in such cases, TDF/FTC as PrEP is contraindicated. (A1)
- Clinicians should not prescribe TAF/FTC as PrEP for any individual with a confirmed CrCl <30 mL/min; in such cases, TAF/FTC as PrEP is contraindicated. (A1)

The 2-drug PrEP regimens of TDF/FTC and TAF/FTC are not adequate for treating established HIV infection; therefore, PrEP should not be initiated unless an individual is tested for HIV within 1 week before proposed initiation.

TDF can cause renal toxicity and is contraindicated for patients with a CrCl <60 mL/min at the time of PrEP initiation [FDA 2016]. There are no data for adjusting TDF dosing in those with an estimated CrCl <50 mL/min. TAF/FTC can be initiated in individuals with a creatinine clearance >30 mL/min and can be used in cisgender MSM and transgender women who have a CrCl <60 mL/min on initiation or a CrCl that drops to <50 mL/min while taking TDF/FTC. Serum creatinine levels can vary and be affected by factors other than renal disease; therefore, before a decision is made to forgo PrEP, decreased CrCl should be verified through repeat testing, and other causes of spurious creatinine elevation (e.g., use of creatine-containing protein supplements) should be ruled out. Potentially reversible causes, such as use of nonsteroidal anti-inflammatory drugs, may be addressed as well. “On-demand” dosing of TDF/FTC may also be considered where appropriate for cisgender MSM with borderline renal function or other kidney disease with a preserved calculated CrCl to decrease drug exposure.

When medication cannot be used for PrEP, education regarding other prevention options, such as condom use and safer sex practices, is essential.

## Pre-Prescription Counseling and Assessment

**→ SELECTED GOOD PRACTICE REMINDERS: Pre-Prescription Counseling and Assessment**

- Assess the patient’s health literacy and ensure that the purpose, benefits, and risks associated with PrEP are understood.
- Individualize the decision to initiate pre-exposure prophylaxis (PrEP) by weighing the benefit of reducing the person’s risk of acquiring HIV against the potential adverse effects of the medication.

### → SELECTED GOOD PRACTICE REMINDERS: Pre-Prescription Counseling and Assessment

- Make clear that PrEP efficacy is highly dependent on adherence; assess for readiness and willingness to adhere to PrEP and recommended follow-up care and assess for barriers to adherence.
- Obtain a thorough sexual history and drug use history, identify risk-taking behaviors, encourage other safer sex practices and, if applicable, safer drug injection techniques.
  - See the NYSDOH AI guidelines *Substance Use Screening and Risk Assessment in Adults* and *Harm Reduction Approach to Treatment of All Substance Use Disorders*.
  - See New York City Department of Health and Mental Hygiene *Making the Sexual History a Routine Part of Primary Care*.
  - See *GOALS: A New Framework for Sexual History Taking in Primary Care*.
- Ask whether the individual has a sex partner (or partners) with known HIV; if yes, ask if the partner’s viral load status is known.
- Discuss with patients in serodifferent partnerships the benefits and risks of relying on their partner’s undetectable viral load achieved with ART alone versus the addition of PrEP for preventing sexual transmission of HIV.
- Counsel serodifferent couples who are considering the use of PrEP during attempts to conceive about the utility, safety, and possible risks of the medication and about other approaches to safer conception.
- Perform a psychosocial assessment and refer for appropriate social and psychological support services, as indicated, to minimize HIV risk and support maintenance in care.

PrEP is an integral part of sexual health and well-being. Developing an HIV prevention plan that includes PrEP offers care providers the opportunity to engage individuals in primary care. Clinicians may use this opportunity to encourage standard, age-appropriate health screenings, immunizations and updates (including hepatitis A/B vaccine, [human papillomavirus vaccine](#) for patients aged ≤45 years, and [meningococcal vaccine](#) when appropriate), screening and brief interventions related to substance use, linkage to specialty services, and other health maintenance activities.

Patient education is vital to shared decision-making and to the success of PrEP as part of a comprehensive HIV prevention plan. Educate PrEP candidates about PrEP risks, benefits, and options. Discuss individual preferences, needs, and circumstances. Adherence may improve when patients participate in medication-related decisions [Johnson, et al. 2012] and are informed about the strong efficacy of PrEP when taken as directed (see [Monitoring and Ongoing Laboratory Testing > Retention in Care](#) and [Adherence](#) in this guideline). Education provided in the individual’s native or preferred language and tailored to the individual’s level of comprehension will help ensure understanding of:

- How PrEP works.
- The benefits and risks of PrEP.
- The need for adherence to the dosing schedule for PrEP to be protective.
- How other safer sex and safer drug injection practices decrease the risk of acquiring drug-resistant HIV, other sexually transmitted infections (STIs), hepatitis C virus, and pregnancy.
  - See [Avert Sex & HIV Fact Sheet](#).
  - See NYSDOH [Syringe Access and Disposal](#).

**Health literacy:** Use a health literacy assessment to evaluate the individual’s knowledge of the:

- Purpose of PrEP.
- Importance of adherence to PrEP.
- Importance of scheduled HIV testing and routine monitoring.
- Potential side effects of PrEP.
- Process for obtaining regular pharmacy refills for PrEP.
- Methods of paying for PrEP or access to payment assistance for PrEP medications and related care services.

→ KEY POINTS

- According to the *National Network of Libraries of Medicine*, health literacy requires:
  - The ability to understand instructions on prescription drug bottles, appointment slips, medical education brochures, and care provider’s directions and consent forms.
  - The ability to negotiate complex healthcare systems.
  - Reading, listening, analytical, and decision-making skills, and the ability to apply these skills to health situations.
- **Resources:**
  - *AHRQ Short Assessment of Health Literacy—Spanish and English*
  - *AHRQ Rapid Estimate of Adult Literacy in Medicine—Short Form*
  - *AHRQ Short Assessment of Health Literacy for Spanish Adults*
  - *Health Literacy Tool Shed (funded by the U.S. National Libraries of Medicine)*

**Sex and drug use history:** A detailed HIV risk assessment includes a patient’s **sexual history** and drug use history, and a frank, open, and nonjudgmental discussion of risk-taking behaviors. As indicated, this discussion may also include the offer of further counseling and referrals, such as for substance use treatment.

- See NYSDOH *Office of Addiction Services and Supports: Treatment*.

**Status of sex partner(s) with HIV:** The antiretroviral treatment and viral load status of a sex partner with HIV may inform the discussion of risk. Sexual transmission of HIV does not occur when an individual with HIV has a persistently undetectable HIV viral load, although an individual without HIV in a serodifferent partnership who does not have HIV may still elect to use PrEP for multiple reasons (see **discussion of U=U** in this guideline) [Rodger AJ, et al. 2016; Zucker HA 2017; Prevention Access Campaign 2019]. If the patient’s partner has detectable virus and genotypic information is not available, knowledge of the partner’s treatment regimen may be useful. A partner with HIV known to be resistant to the components of a PrEP regimen will pose a higher risk of transmission than one without resistance [NYC Health 2016; Knox, et al. 2017], and the individual without HIV should be advised to take additional prevention measures, including condom use.

**Reproductive counseling:** Inquire about the individual’s reproductive plans and provide preconception counseling when indicated. Determine whether the patient or the patient’s partner is pregnant, breastfeeding, intends to conceive, or is currently using contraception, including hormonal contraception or another effective method of contraception, in addition to condoms [Lampe, et al. 2011; Vernazza, et al. 2011; Bujan and Pasquier 2016]. Counsel serodifferent couples who are considering the use of PrEP during attempts to conceive about the utility, safety, and possible risks of the medication (see *Monitoring and Ongoing Lab Testing > Pregnancy Screening and Management* in this guideline).

**Psychosocial assessment:** Assessments of psychosocial needs and challenges, mental health, and substance use are integral to good general medical practice. In the case of someone prescribed PrEP, such assessments enable clinicians to identify modifiable barriers to adherence and to provide services and referrals needed to support adherence and retention in care.

**RESOURCES: PrEP PAYMENT ASSISTANCE**

- For PrEP payment assistance, see NYSDOH *Payment Options for Adults and Adolescents for PrEP* and *PrEP Patient Assistance Program (PrEP-AP)*.
- In July 2019, the New York State Department of Financial Services issued a *Circular Letter* instructing health insurers to provide coverage for PrEP medications without cost-sharing, including co-pays and deductibles.

# Pre-Prescription Medical Evaluation and Laboratory Testing

## RECOMMENDATIONS: Pre-Prescription Medical Evaluation and Laboratory Testing

- Before prescribing pre-exposure prophylaxis (PrEP), clinicians should perform a medical evaluation of the candidate that includes:
  - Assessment for symptoms or signs of acute HIV, including a febrile, flu-like, or mono-like illness in the previous 6 weeks. (A3)
  - Assessment to identify recent risk encounters (<72 hours) and the potential need for post-exposure prophylaxis (PEP) prior to PrEP. (A3)
  - Inquiry about the individual’s reproductive plans. (A3)
  - Evaluation of concomitant medications to identify nephrotoxic drugs or drugs that have interactions with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide (TAF/FTC) as PrEP. (A3)
    - See NYSDOH AI guideline *ART Drug-Drug Interactions*.
  - Laboratory testing listed in *Table 2: Recommended Laboratory Tests to Be Obtained Before Prescribing PrEP* (see ratings in table).
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV > Acute Retroviral Syndrome*.
- Clinicians should prescribe PrEP only after obtaining a specimen for testing using a 4th-generation antigen/antibody (recommended) or 3rd-generation immunoglobulin M (IgM)/IgG antibody (alternative) HIV test and, when appropriate, an HIV viral load test\* within 1 week before planned PrEP initiation. (A3)
  - PrEP may be initiated while results of laboratory-based HIV diagnostic tests are pending unless the individual had a high-risk exposure within the previous 72 hours that requires PEP, has symptoms or signs of acute HIV, or has a history of renal disease or hepatitis B virus. (A2)
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV > Acute Retroviral Syndrome*.
  - Clinicians should assure HIV test results are available and acted upon within 7 days of initiation. (A3)
    - See NYSDOH AI guidelines *Diagnosis and Management of Acute HIV* and *HIV Testing*.

\*Indications for an HIV viral load test: Symptoms of acute HIV in the past 6 weeks or potential injection or sexual exposure in the past 4 weeks.

All individuals who plan to start PrEP should have HIV testing with a 4th-generation antigen/antibody (preferred) or 3rd-generation IgM/IgG antibody (alternative) HIV test within 1 week before PrEP initiation. If a confirmed negative result is not available at the time of the patient’s initial visit, perform rapid HIV testing if available. Question patients about flu- or mono-like symptoms in the past 6 weeks that might indicate acute HIV and about any risk exposures in the prior 4 weeks.

If a patient reports a possible HIV exposure within the previous 4 weeks or reports signs or symptoms consistent with acute infection, then an HIV viral load test should be performed in addition to a 4th-generation HIV test. Before initiating PrEP, it is essential to assess for acute HIV through risk assessment, symptom analysis, and viral load testing when indicated, as use of TDF/FTC or TAF/FTC as PrEP in patients with undiagnosed HIV has led to development of drug-resistant virus [Lehman, et al. 2015; Molina, et al. 2018b].

**Same-day initiation of PrEP:** Once laboratory specimens are obtained, PrEP may be initiated while test results are pending if there are no *symptoms or signs of acute HIV* in the prior 6 weeks, no history of renal disease or hepatitis B virus, and no risk exposures in the past 72 hours requiring PEP, as long as laboratory results will be available and addressed within 7 days. In HIV care, rapid start of treatment has been shown to better engage patients in care [Ford, et al. 2018]. Same-day initiation of PrEP has been shown to be safe, and delayed initiation of PrEP has been associated with a significant rate of loss to follow-up [Mikati, et al. 2019]. Same-day initiation of PrEP may engage patients more fully in care and reduce exposures to HIV while awaiting test results. Same-day PrEP also encourages immediate attention to insurance coverage for PrEP or identification of other options for payment if needed. Same-day initiation of PrEP risks starting a non-suppressive antiretroviral regimen in someone with HIV. However, if laboratory results are available in a

timely manner, then an individual who tests positive for HIV can be started on a fully suppressive antiretroviral treatment regimen and referred for HIV care immediately (see *Managing a Positive HIV Test Result* in this guideline).

Although delays such as insurance barriers may impede initiation of PrEP, the overall goal should be same-day initiation in patients without known hepatitis B, renal disease, need for PEP, or signs or symptoms of acute HIV.

**Initiating PrEP during the window period for HIV testing:** The “window period” is the time between when a person has acquired HIV and when a diagnostic test is able to detect infection. The median time to positivity for an HIV viral load test is 12 days; for a laboratory-based 4th-generation test it is 18 days, but the 99th percentile for a positive test is 33 days for an HIV viral load test and 42 days for a 4th-generation laboratory-based test [Delaney, et al. 2017]. This committee recommends initiating PrEP in individuals tested for HIV even if they are in the window period for detection of HIV seroconversion based on their sexual or drug use exposures, with the understanding that seroconversion may be occurring. Waiting for an individual to be outside of the window period risks additional exposures to HIV and significantly longer delays. Repeat HIV testing at 1 month (see *Monitoring and Ongoing Laboratory Testing* in this guideline) after initiation to help identify potentially positive individuals in a timely manner.

→ KEY POINTS

- Before initiating PrEP, it is essential to assess for acute HIV by identifying high-risk exposures and signs and symptoms of acute retroviral syndrome and performing viral load testing when indicated; use of TDF/FTC or TAF/FTC as PrEP in patients with undiagnosed HIV has led to development of drug-resistant virus [Lehman, et al. 2015; Molina, et al. 2018b; Hare, et al. 2019].
- Same-day initiation of PrEP is the goal whenever possible for appropriately selected patients, including for individuals who may be in the HIV testing window period.

*Table 2: Recommended Laboratory Tests to Be Obtained Before Prescribing TDF/FTC or TAF/FTC as PrEP*, below, lists the laboratory tests that should be performed at the pre-prescription visit for individuals who will initiate PrEP. When an individual is engaged in care to receive PrEP, primary health care may be offered, including vaccinations against hepatitis A and B viruses, human papillomavirus, meningococcus, and influenza, as indicated.

For more information:

- See Centers for Disease Control and Prevention *Recommended Adult Immunization Schedule for Ages 19 Years or Older, United States, 2019*.
- See NYSDOH *Health Advisory: NYSDOH Meningococcal Vaccine Recommendations for HIV-Infected Individuals and Those at High Risk of HIV Infection*.

**Table 2: Recommended Laboratory Tests to Be Obtained Before Prescribing TDF/FTC or TAF/FTC as PrEP**

*Note: PrEP may be initiated while results are pending.*

Test (rating)	Comments
Baseline HIV test (A*)	<ul style="list-style-type: none"> <li>• Obtain a 4th-generation (recommended) or 3rd-generation (alternative) HIV screening test [a].</li> </ul>
HIV RNA testing (A3)	<ul style="list-style-type: none"> <li>• Perform HIV RNA testing [a] in patients who:                             <ul style="list-style-type: none"> <li>– Have had symptoms of acute HIV in the past 6 weeks [Chin, et al. 2013].</li> <li>– Report condomless anal or vaginal sex during the previous 4 weeks.</li> <li>– Have shared injection drug needles in the past 4 weeks.</li> </ul> </li> </ul>
Metabolic panel (A*)	<ul style="list-style-type: none"> <li>• Obtain serum creatinine and calculated CrCl.</li> <li>• TDF/FTC as PrEP should not be initiated in patients with a confirmed calculated CrCl &lt;60 mL/min.</li> <li>• TAF/FTC should not be initiated in patients with a confirmed CrCl &lt;30 mL/min.</li> </ul>
Pregnancy test for all individuals of childbearing capacity (A3)	<ul style="list-style-type: none"> <li>• Discuss the importance of preventing HIV during pregnancy with anyone contemplating pregnancy or who becomes pregnant while taking PrEP. Discuss overall risks and benefits and available data, which suggest that TDF/FTC does not increase risk of birth defects. (See <i>Pregnancy Screening and Management</i> in this guideline.)</li> </ul>

**Table 2: Recommended Laboratory Tests to Be Obtained Before Prescribing TDF/FTC or TAF/FTC as PrEP**

Note: PrEP may be initiated while results are pending.

Test (rating)	Comments
HBV serologies: HBsAg, anti-HBs, and anti-HBc [IgG or total] (A2+)	<ul style="list-style-type: none"> <li>• Vaccinate nonimmune patients (A2).</li> <li>• Chronic HBV: Treat and monitor HBV as per treatment guidelines [b], or refer to an HBV specialist.</li> </ul>
Gonorrhea and chlamydia screening (A2+)	<ul style="list-style-type: none"> <li>• Perform NAATs for gonococcal and chlamydial infections [c] for all patients at all sites of reported exposure.</li> <li>• For all men who have sex with men and transgender women, routinely perform 3-site testing (genital, rectal, and pharyngeal) regardless of sites of reported exposure.</li> <li>• Genital testing [CDC 2014]:                             <ul style="list-style-type: none"> <li>– To detect urethral infection, urine specimens are preferred over urethral specimens.</li> <li>– For vaginal/cervical testing, vaginal swabs are preferred over urine-based testing.</li> <li>– For transgender women with a neovagina, there are insufficient data to make a recommendation regarding urine-based testing vs. vaginal swab [d].</li> </ul> </li> <li>• Self-collected swabs from the <b>pharynx</b>, <b>vagina</b>, and <b>rectum</b> are reasonable options for patients who may prefer them over clinician-obtained swabs. [Geelen, et al. 2013; Paudyal, et al. 2015].                             <ul style="list-style-type: none"> <li>○ See <i>STI Screening</i> in this guideline for further details.</li> </ul> </li> </ul>
Syphilis screening (A2+)	<ul style="list-style-type: none"> <li>• Screen for syphilis [e] according to the laboratory’s testing algorithm.                             <ul style="list-style-type: none"> <li>○ See <i>Standard Protocol for Syphilis Screening and Diagnosis</i> and <i>Alternative, Reverse Algorithm for Syphilis Screening and Diagnosis</i>.</li> </ul> </li> </ul>
HCV serology (A3)	<ul style="list-style-type: none"> <li>• Inform patients with HCV about the risk of transmission and offer or refer for treatment.                             <ul style="list-style-type: none"> <li>○ See the NYSDOH AI guideline <i>Treatment of Chronic HCV with Direct-Acting Antivirals</i>.</li> </ul> </li> </ul>
HAV serology (good practice)	<ul style="list-style-type: none"> <li>• Obtain for individuals at high risk for HAV, including MSM and those who:                             <ul style="list-style-type: none"> <li>– Have chronic liver disease or conditions that can lead to chronic liver disease (e.g., chronic HBV, chronic HCV, alcohol use, or genetic liver diseases).</li> <li>– Are travelers to or from countries with high or intermediate endemicity of HAV infection.</li> <li>– Use illicit drugs, particularly injection drugs.</li> <li>– Are unstably housed/homeless.</li> <li>– Live in a community identified by the local health department as experiencing an outbreak of HAV infection.</li> <li>– Have clotting-factor disorders.</li> <li>– Want to reduce their risk for HAV infection.</li> <li>– Are at occupational risk and are not otherwise required to receive HAV vaccination.</li> <li>– Are at risk of HAV-related morbidity or mortality.</li> </ul> </li> <li>• Vaccinate nonimmune patients.</li> </ul>
Serum liver enzymes (good practice)	<ul style="list-style-type: none"> <li>• Increased serum liver enzymes may indicate acute or chronic viral hepatitis infection and require further evaluation.</li> </ul>
Urinalysis (good practice)	<ul style="list-style-type: none"> <li>• As part of standard primary care, urinalysis is used to identify preexisting renal disease, proteinuria, and glycosuria.</li> <li>• Only calculated CrCl is used to guide decisions regarding use of TDF/FTC and TAF/FTC as PrEP based on renal function.</li> </ul>

**Abbreviations:** anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; CrCl, creatinine clearance; GFR, glomerular filtration rate; HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; IgG, immunoglobulin G; MSM, men who have sex with men; NAAT, nucleic acid amplification test; STI, sexually transmitted infection; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.

**Notes:**

- See NYSDOH AI guideline *HIV Testing*.
- See NYSDOH AI guideline *HBV-HIV Coinfection*.
- See NYSDOH AI guideline *Management of Gonorrhea and Chlamydia in Patients with HIV*.
- See UCSF *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People*.
- See NYSDOH AI guideline *Management of Syphilis in Patients with HIV*.

# Prescribing PrEP

## RECOMMENDATIONS: Prescribing PrEP

- Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) is the preferred regimen for pre-exposure prophylaxis (PrEP). Clinicians should prescribe TDF 300 mg/FTC 200 mg once daily with or without food as PrEP. (A1)
  - Tenofovir alafenamide/emtricitabine (TAF/FTC) once daily is an option for prevention of HIV through sexual exposure in cisgender MSM and transgender women. TAF 25 mg/FTC 200 mg is not a recommended option for sexual exposure through receptive vaginal sex.
  - TAF/FTC as PrEP is preferred in cisgender MSM and transgender women who have preexisting renal disease or osteoporosis.
- If daily dosing is a barrier to adherence or if episodic dosing is preferred, clinicians should evaluate the appropriateness of on-demand dosing of TDF/FTC as PrEP. (A3)

## Preferred Regimen

TDF/FTC is the preferred PrEP regimen because of its proven efficacy and safety in trials as well as its suitability for use as PrEP across all populations. TAF/FTC is an alternative option for men who have sex with men (MSM) and transgender women and is preferred in cisgender MSM and in transgender women with preexisting renal disease or osteoporosis, and may also be preferable in individuals with multiple risk factors for the development of either renal disease or osteoporosis.

## Dosing Strategies

**Daily versus on-demand dosing:** The dosing of TDF/FTC as PrEP approved by the U.S. Food and Drug Administration is 1 pill daily with or without food [FDA 2016]. Alternative dosing strategies, such as on-demand PrEP (also called intermittent, event-driven, or coitally timed PrEP) have been studied. The IPERGAY [Molina, et al. 2015] and Prevenir [Molina, et al. 2018b] studies found that on-demand dosing (with 2 TDF/FTC tablets 2 to 24 hours before sex and 1 additional tablet at 24 and 48 hours after sex, also called “2-1-1 dosing”) effectively prevented HIV acquisition in men who have sex with men (MSM). Concerns have been raised as to whether the efficacy observed in the IPERGAY study was a result of the frequency of dosing when PrEP was used on demand. The average number of PrEP doses taken per month by participants in the IPERGAY study was 15 (approximately 4 pills per week) [Molina, et al. 2015], which was the minimum level of adherence necessary for protection in the iPrEx study [Anderson, et al. 2012]. The iPrEx-OLE study, an open-label extension of the iPrEx study [Grant RM, et al. 2010], confirmed that 4 or more doses of TDF/FTC as PrEP per week was protective for men enrolled in the study [Grant RM, et al. 2014]. However, in a sub-study of IPERGAY, PrEP dosed on demand remained effective even in those with less frequent sexual activity [Antoni, et al. 2017]. The HPTN 067 ADAPT study investigated daily versus time-driven (twice per week with an additional dose after sex) versus event-driven dosing and found that adherence with event-driven dosing was lower than daily dosing in the men and women studied [Mannheimer, et al. 2015]. On-demand dosing has not been studied for TAF/FTC; this regimen should not be dosed on demand in any population.

**On-demand dosing in different populations:** The effectiveness of on-demand TDF/FTC as PrEP in women has not been established. In the HPTN 067 ADAPT study, levels of orally administered tenofovir were much lower in the vagina than in the anal compartment [Anderson, et al. 2016]. Further data suggest that vaginal sex requires nearly 100% adherence to PrEP to achieve protective levels [Cottrell, et al. 2016]. Because of the differential pharmacokinetics for vaginal exposure with TDF/FTC as PrEP, on-demand dosing of PrEP cannot be recommended for cisgender women or transgender men having receptive vaginal sex without further data. Data are also lacking for men who have sex with women.

In people who inject drugs, it appears that rates of adherence to PrEP must be higher than those of other populations to confer protection, based on the Bangkok Tenofovir Trial (TDF alone) [Choopanya, et al. 2013], and on-demand dosing cannot be recommended in this population. Lower tenofovir concentrations have been observed in transgender women who take estrogen (area under the curve [AUC], 13%; C<sub>24</sub>, 17%) [Hiransuthikul, et al. 2018; Cottrell, et al. 2019], which may indicate that a higher level of adherence is needed for protection in transgender women taking TDF/FTC as PrEP; this may obviate on-demand dosing in this population as well.

For cisgender MSM, the data on daily dosing of TDF/FTC are more robust than for on-demand dosing, with longer follow-up. Daily dosing remains the preferred dosing strategy. However, on-demand dosing with TDF/FTC is an option when lifestyle, sexual practices, or stated preferences make it a more acceptable choice as long as they are hepatitis B negative. As mentioned above, on-demand dosing is 2 TDF/FTC tablets 2 to 24 hours before sex (closer to 24 hours is preferred), followed by 1 TDF/FTC tablet at 24 and 48 hours after sex (also called “2-1-1 dosing”). If sex occurs again during this interval, the daily dosing is continued until 48 hours after the last sexual act, effectively becoming daily PrEP as long as sex continues. Because on-demand dosing requires planning of sex by at least 2 hours to be successful, ask patients to review their usual practices around planning for sex to help them assess the feasibility of this approach. Logistical challenges in prescribing on-demand PrEP exist, such as ensuring understanding of a more complex dosing strategy, and decisions regarding amount of medication to prescribe when not taken daily, but should not preclude the use of this strategy when it is appropriate. Switching back and forth between daily and on-demand PrEP may be an appealing, evidence-based option for some individuals [Hoorneborg, et al. 2017a; Molina, et al. 2018b]. On-demand dosing is currently recommended as an alternative PrEP strategy for MSM by the [International Antiviral Society–USA](#), [British HIV Association \(BHIVA\)](#), [European AIDS Clinical Society](#), [World Health Organization \(WHO\)](#), and [New York City Department of Health and Mental Hygiene](#).

**Episodic PrEP use:** For some individuals, HIV risk is “episodic.” A person may engage in risk behaviors only while on vacation or may engage in sexual activity only with a long-distance partner during periodic visits. In these and similar circumstances, it may be appropriate for an individual, regardless of type of risk exposure, who is negative for hepatitis B to choose to use PrEP only during periods of need, as long as it is initiated early enough to reach protective levels prior to exposure (see *Time to Protection*, below) [Elsesser, et al. 2016].

#### → KEY POINTS

- Daily dosing of PrEP is the preferred dosing regimen.
- On-demand PrEP with TDF/FTC is an option for cisgender MSM, although daily dosing is the preferred strategy based on robust existing data.
- On-demand dosing of TAF/FTC for PrEP has not been studied; TAF/FTC should not be dosed in this way.
- On-demand PrEP is *not* recommended for:
  - Transgender women who take estrogen.
  - Individuals who engage in vaginal sex.
  - Individuals who use injection drugs.
  - Individuals with hepatitis B virus.
- Use of PrEP only during discrete periods of risk is a reasonable alternative to ongoing daily PrEP when risk is episodic.

## Time to Protection

The time to protection against HIV infection after PrEP initiation is not definitively established. No studies have directly assessed time to protection, and the site of PrEP action in blood, rectal, and genital tissue has not been settled. Most of what is known is from animal studies, human tissue studies, and pharmacokinetic modeling. There are no studies with clinical endpoints. Adding more uncertainty to the question of what correlates with time to protection in PrEP dosing is the efficacy of post-exposure prophylaxis (PEP), which in animal models and observational studies has been effective if initiated 36 to 72 hours after exposure. This raises questions about the need to achieve specific drug concentrations in tissue in advance of exposure in order to protect against HIV infection.

Earlier pharmacokinetic modeling data demonstrated that 7 days of daily dosing of TDF/FTC for PrEP are required to achieve maximal protective concentrations in anal tissue, and 20 days of daily dosing are required to achieve maximal protective concentrations in cervicovaginal tissue [Patterson, et al. 2011; Anderson, et al. 2012; Louissaint, et al. 2013]. No data are available on protective concentrations of TDF/FTC in penile tissue. Based on these results, the [Centers for Disease Control and Prevention](#) and the [NYSDOH AI 2017 PrEP guidelines](#) recommended 7 days of TDF/FTC as PrEP for rectal exposure and 20 days of PrEP for vaginal, penile, and injection exposures to achieve protection.

More recent data and modeling suggest that the onset of protective effect is likely within 1 week of dosing in rectal and genital compartments and in peripheral blood mononuclear cells (PBMCs) [Hendrix, et al. 2016; Seifert, et al. 2016]. It has also been shown that FTC-TP (active metabolite of FTC) reaches steady state and therapeutic concentrations very quickly in vaginal tissue, while TFV-DP (active metabolite of TFV) reaches concentrations more slowly, potentially affording

vaginal protection quite early from FTC-TP while awaiting TFV-DP concentrations to accumulate [Cottrell, et al. 2016; Seifert, et al. 2016]. Based on these data, some guidelines suggest shorter intervals to PrEP protection with TDF/FTC: both the 2017 WHO and the 2018 BHIVA guidelines recommend 7 days PrEP lead-in for protection via vaginal and injection exposure [WHO 2017; Brady, et al. 2018]. The WHO guideline recommends a time to protection of 7 days for all sites of exposure, but the BHIVA guideline advises that rectal protection is achieved 24 hours after an initial double (loading) dose, based on the efficacy shown in the IPERGAY study and pharmacokinetics indicating achievement of protective concentrations of TDF/FTC sooner with a loading dose. Although concrete guidance on efficacy would be best, and accumulating evidence points to an earlier time to protection for vaginal exposure, a definitive answer to this question is not yet available, and experts disagree in their interpretation of the evidence [AVAC 2017].

Time to protection for TAF/FTC is also unclear. TAF had a faster time to effective concentrations (EC90) than TDF (4 hours vs. 3 days) and significantly higher steady state concentrations in PBMCs in a group of healthy volunteers than TDF/FTC as PrEP [Spinner, et al. 2019], which may confer a clinical benefit in terms of time to protection and adherence forgiveness, but this is preliminary evidence that needs further evaluation.

Given this uncertainty, clinicians should advise patients that time to protection from PrEP is not definitely known. The most conservative counseling is that after 7 days of daily dosing of TDF/FTC optimal protection is achieved for rectal exposure and is most likely achieved for genital and blood exposure, and after 20 days of daily dosing optimal protection is achieved for all sites of exposure. Additionally, studies in cisgender MSM have demonstrated that on-demand dosing of PrEP is effective; therefore, protection may be established in cisgender MSM with a loading dose of 2 pills of TDF/FTC prior to any risk exposure. By extension, taking 2 pills of PrEP on the day of initiation might decrease the time needed to achieve protective concentrations for all sites of exposure, although it is not known by how much other than in cisgender MSM. Data are insufficient to make a recommendation regarding time to protection for TAF/FTC.

#### → KEY POINTS

- Time to protection is based on pharmacokinetic modeling studies and has not been clinically determined.
- For rectal exposure, protection against HIV acquisition is achieved after 7 days of TDF/FTC daily dosing and possibly earlier.
- For genital and blood exposure, protection against HIV acquisition is likely achieved after 7 days of TDF/FTC daily dosing, but optimal drug concentrations are achieved after 20 days of daily dosing.
- Taking 2 pills of TDF/FTC as PrEP on the day of initiation will decrease the time needed to achieve protective drug concentrations for all sites of exposure.
- Data are insufficient to make an estimate regarding time to protection for TAF/FTC.

# Monitoring and Ongoing Laboratory Testing

## RECOMMENDATIONS

### Monitoring

- Clinicians should perform routine monitoring of patients using pre-exposure prophylaxis (PrEP) according to the recommendations in *Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP* (see table for ratings). **HIV Testing**
- Clinicians should:
  - Obtain a 4th-generation (recommended) or 3rd-generation (alternative) laboratory-based HIV screening test before initiation of PrEP. (A\*)
  - Repeat HIV testing 1 month after initiation for those reporting a risk exposure in the 30 days prior to PrEP initiation. (A2<sup>+</sup>)
  - Perform HIV testing every 3 months while a patient is using PrEP. (A3)
- If a patient presents with symptoms or signs of a flu-like illness consistent with possible acute retroviral syndrome, clinicians should perform HIV testing immediately according to guidelines for the evaluation of acute HIV, including an HIV viral load test and a laboratory-based 4th-generation HIV test. (A2)
  - See *Managing a Positive HIV Test Result* in this guideline and the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*.

### Renal Function Testing

- At the following intervals, clinicians should perform renal function testing, including testing serum creatinine level and calculated creatinine clearance (CrCl) :
  - Before initiating PrEP with tenofovir disoproxil fumarate (TDF/FTC) or tenofovir alafenamide/emtricitabine TAF/FTC. (A\*)
  - At 3 months after initiation. (B3)
  - At least every 6 months for the duration of use of TDF/FTC or TAF/FTC as PrEP; more frequent screening may be required in patients at higher risk for renal disease. (A3)
- Clinicians should discontinue daily TDF/FTC as PrEP if a patient develops a confirmed calculated CrCl <50 mL/min and consider other alternative dosing and options; see discussion in text for strategies and options for patients with reduced renal function. (A3)
- Clinicians should perform urinalysis at baseline and annually, assessing for urine glucose and protein. (B3)

### Sexually Transmitted Infection (STI) Screening

- At every visit, a care team member should assess patients for signs and symptoms of STIs, including syphilis and gonococcal and chlamydial infections, as part of a sexual history and treat these infections empirically based on symptoms while results are pending. (A2<sup>+</sup>)
- Clinicians should perform ongoing testing for syphilis and gonococcal and chlamydial infections every 3 months at all sites of exposure, regardless of symptoms, as specified in *Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP*. (A2<sup>+</sup>)

### Hepatitis C Virus (HCV) Screening

- Clinicians should obtain at least annual HCV testing for at-risk patients using PrEP. (A3)

### Pregnancy Screening and Management

- Clinicians should assess for possibility of pregnancy in individuals of childbearing potential at every visit. (A3)

→ SELECTED GOOD PRACTICE REMINDERS

**Monitoring and Ongoing Laboratory Testing**

- Upon initiation of PrEP, clinicians should instruct patients to notify their care provider immediately if they experience side effects.
- Within 2 weeks of PrEP initiation, a member of the care team should follow up to ensure the following:
  - The patient has filled the prescription for PrEP and understands how to take the medication.
  - Any problems with payment for PrEP are identified and solved.
  - Side effects, if any, are addressed and assistance with management is provided.
- At each visit, clinicians should:
  - Assess adherence and discuss strategies for maintaining adherence.
  - Discuss risk reduction in the context of the individual’s sexual health or injection drug use.
  - Offer condoms and, if appropriate, syringe access.
  - Inquire about side effects and offer advice for management if needed.
- Clinicians should follow the schedule of visits detailed in the *PrEP Management Checklist*.

**Adherence and Retention in Care**

- Clinicians should:
  - Provide adherence counseling during every patient contact.
  - Partner with care providers within or outside of their organization to provide services, including subspecialty services, mental health and substance use treatment, case management, navigation and linkage services, housing assistance, and income/benefits assessments.
  - Explore and address potential barriers to ongoing use of and adherence to PrEP.
  - Make every effort to avoid discontinuing PrEP or withholding it from a patient at risk of acquiring HIV.

**Risk Reduction**

- At every patient encounter, clinicians should offer female/receptive or male/insertive condoms to help decrease the patient’s risk of acquiring HIV and other sexually transmitted infections (STIs).
- For patients who inject drugs or misuse mood-altering drugs, clinicians should:
  - Refer for substance use treatment and mental health support as appropriate.
  - Prescribe clean syringes and needles or refer to needle-exchange programs as indicated. See NYSDOH *Expanded Syringe Access Program* and *Syringe Exchange Programs*.

Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP, below, lists the laboratory tests that should be performed for individuals who are taking PrEP.

<b>Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP</b>	
<i>Note: Recommended testing does not have to be linked to an office or clinic visit.</i>	
<b>Monitoring or Laboratory Testing (rating)</b>	<b>Frequency (rating)</b>
HIV testing [a]: 4th-generation (recommended) or 3rd-generation assay (alternative) HIV screening test	<ul style="list-style-type: none"> <li>• 1 month after initiation for individuals with risk exposure within 1 month prior to PrEP initiation. (A2<sup>+</sup>)</li> <li>• Every 3 months while a patient is using PrEP. (A3)</li> </ul>
HIV serology screening test plus HIV RNA test [a]	<ul style="list-style-type: none"> <li>• When a patient has:                             <ul style="list-style-type: none"> <li>– Symptoms of acute HIV [b]. (A2)</li> <li>– When there has been an interruption in PrEP in the past month and a potential exposure has occurred. (A3)</li> </ul> </li> </ul>

**Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP**

*Note: Recommended testing does not have to be linked to an office or clinic visit.*

Monitoring or Laboratory Testing (rating)	Frequency (rating)
Serum creatinine and calculated creatinine clearance	<ul style="list-style-type: none"> <li>• 3 months after initiation (B3) and every 6 months thereafter while taking TDF/FTC or TAF/FTC as PrEP. (A3)</li> <li>• Consider more frequent screening in those at higher risk (e.g., age &gt;40 years, other comorbidities). (A3)</li> </ul>
STI screening (A2+): <ul style="list-style-type: none"> <li>• Ask about STI symptoms</li> <li>• Test for syphilis</li> <li>• Test for gonococcal and chlamydial infections</li> <li>• Test and empirically treat all symptomatic patients for STIs</li> </ul>	<ul style="list-style-type: none"> <li>• Ask about symptoms at every visit.               <ul style="list-style-type: none"> <li>– For patients who present with symptoms, perform STI testing and treat as appropriate.</li> </ul> </li> <li>• Test for syphilis, gonorrhea, and chlamydia every 3 months regardless of symptoms and on patient request. Frequency can be adjusted based on risk assessment and occur less often in patients at lower risk of exposure.</li> <li>• Perform NAATs for gonococcal and chlamydial infections for all patients at all sites of reported exposure.</li> <li>• For all MSM and transgender women, routinely perform 3-site testing (genital, rectal, and pharyngeal) regardless of sites of reported exposure unless declined.</li> <li>• Genital testing:               <ul style="list-style-type: none"> <li>– To detect urethral infection, urine specimens are preferred over urethral specimens.</li> <li>– For vaginal/cervical testing, vaginal swabs are preferred over urine-based testing.</li> <li>– For transgender women with a neovagina, data are insufficient to make a recommendation regarding urine-based testing vs. vaginal swab.</li> </ul> </li> <li>• Self-collected swabs from <b>pharynx</b>, <b>vagina</b>, and <b>rectum</b> are reasonable options for patients who may prefer them over clinician-obtained swabs.</li> </ul>
HCV serology [c] (A3)	<ul style="list-style-type: none"> <li>• At least annually for those at risk.</li> </ul>
Pregnancy screening in individuals of childbearing potential (A3)	<ul style="list-style-type: none"> <li>• Assess for possibility of pregnancy at every visit.</li> <li>• Offer birth control when appropriate.</li> <li>• Test for pregnancy when appropriate and on patient request.</li> </ul>
Urinalysis (B3)	<ul style="list-style-type: none"> <li>• Annually.</li> </ul>
<p><b>Abbreviations:</b> HCV, hepatitis C virus; MSM, men who have sex with men; NAAT, nucleic acid amplification test; STI, sexually transmitted infection; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.</p> <p><b>Notes:</b></p> <p>a. See the NYSDOH AI guideline <a href="#">HIV Testing</a>.</p> <p>b. See the NYSDOH AI guideline <a href="#">Diagnosis and Management of Acute HIV</a>.</p> <p>c. See the NYSDOH AI guideline <a href="#">Treatment of Chronic HCV With Direct-Acting Antivirals</a>.</p>	

## Retention in Care

Retention in care is a challenge for PrEP programs. A study that examined PrEP programs in 3 midsized cities found the rate of retention in PrEP care at 6 months to be 60% due to individual and structural barriers [Chan, et al. 2016]. “Over medicalization” of PrEP care may pose a barrier to retention by requiring healthy individuals to engage frequently with health care through quarterly clinic visits and laboratory tests. Although quarterly assessments remain the standard for PrEP monitoring, flexibility regarding in-person visits is encouraged when needed or appropriate. Quarterly laboratory testing is recommended even when a decision to adjust visit frequency has been made, but flexibility for individual patients regarding this time frame is appropriate, as quarterly screening is based on best practice rather than evidence. Barriers to retention in care should be explored with all patients, and individualized solutions should be explored with those who are struggling to remain in care but who wish to continue PrEP use. Novel models, such as annual visits with quarterly at-home HIV testing [Siegler, et al. 2019], are promising, and transition to telemedicine programs should be explored where appropriate as a way to remove structural barriers for patients having difficulty with PrEP persistence.

Provision of gender-affirming care and transition-related care to transgender individuals may also increase PrEP uptake and retention in care [Sevelius, et al. 2016]. Clinicians should partner with care providers within or outside of their organization to provide services, including subspecialty services, mental health and substance use treatment, case management, navigation and linkage services, housing assistance, and income/benefits assessments. Refer patients to support groups if indicated. However, PrEP should not be withheld from individuals who are not interested in engaging in primary care or who may choose to obtain PrEP from a location different from where they receive primary care.

#### → KEY POINT

- Flexibility regarding frequency of in-person visits may help improve PrEP uptake and persistence in care.

## Adherence

In studies of TDF/FTC as PrEP, efficacy was highly dependent on adherence [Sidebottom, et al. 2018]. Some reasons for decreased adherence are side effects, fear of long-term toxicity, perceived low risk of infection, insurance issues, and difficulty with daily dosing. For patients who struggle with adherence to PrEP, strategies such as more frequent visits or contact with medical and nonmedical care providers may be helpful. Adherence decreased when visits went from monthly to quarterly in adolescent patients [Hosek, et al. 2017]. Assessing and addressing individual reasons for suboptimal adherence to PrEP is important [Jenness, et al. 2016; Goodreau, et al. 2018].

Transgender women may avoid PrEP or miss doses because they believe that drugs active against HIV lower estrogen levels. A recent study confirmed that TDF/FTC does not lower estrogen levels [Hiransuthikul, et al. 2018], and addressing this directly with transgender women and providing reassurance regarding estrogen levels may improve their willingness to take and adhere to PrEP. Currently, there are no data available regarding the effect of TAF/FTC on estrogen levels.

Some care providers use peer supporters to reinforce adherence to medication and appointments. If patients are consistently unable to adhere to the regimen despite interventions to improve adherence or if they decline to take PrEP daily, it may be appropriate to explore alternative dosing schedules, such as on-demand PrEP (for cisgender MSM only, with TDF/FTC) or seasonal or vacation use of PrEP (see *Prescribing PrEP > Dosing Strategies* in this guideline). It may also be appropriate to discuss stopping PrEP and using other risk-reduction strategies that better meet the needs of the individual.

The degree of adherence to PrEP required to prevent HIV varies by site of exposure. Based on modeling studies of rectal exposure, 4 doses per week of TDF/FTC appears sufficient to protect against HIV [Grant RM, et al. 2014]; however, modeling studies also suggest that vaginal and injection HIV exposures require closer to 7 doses of TDF/FTC per week for efficacy [Patterson, et al. 2011; Choopanya, et al. 2013; Cottrell, et al. 2016]. There are no data on adherence needed for penile insertive exposure. Currently, there are no data available regarding levels of adherence required for TAF/FTC effectiveness.

#### → KEY POINTS

- Education regarding the importance of and strategies to support PrEP adherence may improve adherence to PrEP and recommended monitoring.
- The minimum degree of adherence to TDF/FTC as PrEP required for protection against HIV varies by site of exposure. Nevertheless, a high degree of adherence is important.
- Use of TDF/FTC does not lower estrogen levels, and addressing this directly with transgender women may improve willingness to take and adhere to PrEP.
- Data regarding degree of adherence needed for TAF/FTC as PrEP and the effect of TAF/FTC on estrogen levels are not currently available.

## Risk Reduction

Clinicians should encourage condom use [Van de Perre, et al. 1987], safer sex practices, and if applicable, safer injection techniques [Abdul-Quader, et al. 2013; Jarlais 2013; Bramson, et al. 2015] at every visit. Discussions about risk reduction should be tailored to patients' specific needs.

If patients have partners with HIV, clinicians should emphasize that transmission does not occur if the individual with HIV in a serodiscordant partnership has a consistently suppressed viral load on treatment [Rodger AJ, et al. 2016]. Clinicians may explore treatment barriers for the partner with HIV. (See NYSDOH AI *U=U Guidance for Implementation in Clinical Settings.*)

## Side Effects

In clinical trials of TDF/FTC as PrEP, the most common side effects associated with TDF/FTC were mild and short-lived: predominantly nausea, headache, abdominal pain, and dizziness [Grant RM, et al. 2010; Thigpen, et al. 2012; McCormack, et al. 2016]. Most side effects peaked at 1 month and generally resolved within 3 months [Glidden, et al. 2016]. In a recent study comparing TAF/FTC and TDF/FTC, both regimens were well tolerated, with diarrhea the only side effect in >10% of individuals in either arm [Hare, et al. 2019].

Two weeks after PrEP initiation, a care team member should follow up either in person or by telephone to assess and address side effects by helping patients manage side effects until they abate. Gastrointestinal side effects can be alleviated by taking PrEP with food or with antidiarrheal agents, anti-gas medications, and antiemetics as needed. In the iPrEx [Grant RM, et al. 2010; Grant RM, et al. 2014] and Partners [Mujugira, et al. 2016] trials of TDF/FTC as PrEP, rash was not reported as a common side effect. Patients who develop a rash while on TDF/FTC or TAF/FTC as PrEP should be assessed for syphilis and acute HIV [Apoola, et al. 2002].

Renal impairment and loss of bone density have been observed in individuals taking TDF/FTC as treatment for HIV, predominantly in studies in which TDF/FTC was combined with a third drug containing the pharmacokinetic booster ritonavir or cobicistat. Studies comparing unboosted TDF/FTC and TAF/FTC for HIV treatment found no difference in adverse events between the 2 arms [Hill, et al. 2018]. A recent meta-analysis of 13 trials of TDF/FTC used as PrEP found no difference in serious adverse events between TDF/FTC and placebo. It did find a borderline statistically significant difference in creatinine elevation of all grades when comparing TDF/FTC with placebo and adding in grade 1 and 2 elevations. The DISCOVER study, which compared TDF/FTC with TAF/FTC for PrEP, did find a small but statistically significant difference between biomarkers of renal and bone dysfunction favoring TAF/FTC, although no difference was found in clinical adverse outcomes [Hare, et al. 2019]. Although renal dysfunction is uncommon, especially in younger patients on TDF/FTC as PrEP [Gandhi, et al. 2016], regular laboratory monitoring is necessary during use of TDF/FTC or TAF/FTC (see *Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP*, above). If an increase in serum creatinine or a decrease in calculated creatinine clearance (CrCl) is observed, evaluate potential causes other than TDF or TAF use. Discontinuation or interruption of TDF/FTC as PrEP is appropriate if other causes are ruled out or the CrCl drops to <50 mL/min (confirmed on 2 readings) for any reason. TAF/FTC is indicated for cisgender men who have sex with men (MSM) and transgender women with CrCl >30 mL/min. On-demand dosing of TDF/FTC can also be considered where appropriate for MSM with borderline renal function to decrease drug exposure.

Bone density losses with use of TDF/FTC as PrEP are minimal and have not been associated with bone fractures [Havens, et al. 2019; Spinelli, et al. 2019]. No additional monitoring of bone mineral density is recommended. For cisgender MSM and transgender women already at high risk of fracture due to osteoporosis, use of TAF/FTC may be considered.

### → KEY POINTS

- Side effects associated with TDF/FTC and TAF/FTC used as PrEP are generally mild and resolve within 3 months after initiation [Pilkington, et al. 2018; Hare, et al. 2019].
- In clinical trials, rash was not a commonly observed side effect among participants taking TDF/FTC as PrEP [Grant RM, et al. 2010; Mujugira, et al. 2016] and should prompt assessment for syphilis and acute HIV [Apoola, et al. 2002] (see *Managing a Positive HIV Test Result* in this guideline).
- TAF/FTC is an alternative to TDF/FTC in MSM and transgender women who are at risk for or exhibit renal or bone toxicity.

## HIV Testing

**Routine testing:** HIV testing every 3 months for individuals taking PrEP is recommended to ensure early detection of PrEP failure, and vigilance for signs and symptoms of potential HIV seroconversion is crucial. The 2-drug TDF/FTC and TAF/FTC PrEP regimens are not adequate for treatment of acute or chronic HIV, and continued use of these regimens in the presence of HIV may lead to viral resistance to these drugs. Nonetheless, required quarterly HIV testing is based on best

practice rather than evidence. If a patient is unable to be tested on this schedule, every effort should be made to avoid interruption of PrEP. One possible strategy is to provide an additional month of PrEP and devise a plan for HIV testing as soon as possible.

Although monitoring and HIV and STI testing every 3 months are recommended, an in-office visit is not required to prescribe PrEP and may create a barrier to PrEP access for some individuals. It is reasonable for patients established on PrEP to be tested every 3 months either on-site or at an outside laboratory, and seen every 6 to 12 months. Alternative monitoring models, such as home testing and telehealth, may decrease barriers to access and monitoring.

**Testing if an HIV exposure is suspected:** For patients who present for PrEP initiation but have had a recent potential exposure (in the past 30 days) in which the initial HIV testing may not detect early infection, repeat HIV testing at 1 month post-initiation is recommended to rule out early HIV infection.

If acute HIV is suspected [Apoola, et al. 2002; Chin, et al. 2013], the clinician should perform an HIV serologic screening test in conjunction with a plasma HIV RNA assay. Even if 4th generation rapid test is performed, a laboratory-based 4th-generation HIV antigen/antibody combination test is the recommended serologic screening test for acute infection. Detection of HIV RNA or antigen in the absence of serologic evidence of HIV should be considered a preliminary positive result. For information about what to do when the HIV test of a patient receiving PrEP is reactive, see *Managing a Positive HIV Test Result* in this guideline.

For more detailed recommendations on testing for acute HIV, see the NYSDOH AI guidelines *Diagnosis and Management of Acute HIV* and *HIV Testing*.

#### → KEY POINTS

- Routine HIV testing is an integral component of the safe use of PrEP.
- HIV testing does not have to be linked to an in-office visit.
- If an individual taking PrEP misses a scheduled testing appointment, do not interrupt PrEP. Instead, encourage continuation of PrEP and work with the individual to reschedule any necessary visits or laboratory testing.
- Frequent screening for HIV infection is performed to prevent development of drug-resistant virus and to protect against transmission of HIV if HIV seroconversion has occurred.

## Renal Function Testing

One sign of tenofovir toxicity is the development of proteinuria. A baseline urinalysis helps to identify preexisting proteinuria before initiating PrEP. Periodic renal function monitoring is also important while a patient is taking TDF/FTC or TAF/FTC as PrEP. An elevated creatinine level should prompt an assessment for causes of renal dysfunction other than tenofovir and an assessment for possible spurious elevation caused by use of creatine supplements.

Renal toxicity is more likely to occur in individuals aged >40 years [Gandhi, et al. 2016]. More frequent creatinine screening may be appropriate for such individuals or for those with comorbidities, such as diabetes or hypertension, or who are taking concomitant nephrotoxic drugs that might place them at higher risk for renal dysfunction.

## STI Screening

**Sexual risk behavior and PrEP utilization:** Risk compensation—an increase in sexual behaviors with an increased risk of STI contraction, such as decreased condom use or increased number of sexual partners—can lead to an increase in STI incidence and is sometimes cited by care providers as a reason not to offer PrEP.

A meta-analysis of 20 studies [Werner, et al. 2018] found that rates of sexual risk behaviors and STIs in MSM taking PrEP remained stable or decreased in the majority of the studies. In a separate meta-analysis limited to open-label studies in which participants knew they were receiving active drug [Traeger, et al. 2018], a majority of studies reported an increase in condomless sex but no significant increase in the proportion of MSM participating in condomless sex, indicating that participants were not using condoms consistently before they started PrEP.

High baseline STI rates in participants in PrEP trials demonstrate that risk behavior often precedes engagement in PrEP care. Initiating PrEP care for individuals who are at risk for HIV provides an opportunity for routine STI monitoring and treatment. One modeling study demonstrated that increased PrEP engagement along with routine STI screening and treatment would lower STI rates through detection and treatment of asymptomatic STIs that might otherwise remain

undiagnosed [Jenness, et al. 2017]. Modeling indicated that STI rates decline more rapidly as higher numbers of at-risk individuals initiate PrEP and related STI screening services, with an even greater reduction in STIs the more frequently STI testing occurs, even in the event of a 40% to 80% decrease in condom use [Jenness, et al. 2017].

**STI testing:** Many patients who elect to initiate PrEP are at high risk of acquiring STIs, including syphilis and gonorrheal and chlamydial infections. Data from New York State and other jurisdictions show high rates of STIs, a majority of which are asymptomatic, making inquiry about symptoms insufficient, and supporting testing for syphilis and gonococcal and chlamydial infections at quarterly intervals [Liu A, et al. 2015; Cohen S, et al. 2016; Golub, et al. 2016]. Less frequent testing can be considered for individuals at lower risk of acquiring STIs. However, frequent testing leads to early diagnosis and treatment of asymptomatic STIs and has the potential to decrease development of complicated infections, such as neurosyphilis or pelvic inflammatory disease, and decrease transmission to sex partners.

Syphilis serologic testing should be performed for all patients taking PrEP, and all patients should be asked about anatomic sites of potential exposure and screened for gonococcal and chlamydial infections accordingly. MSM and transgender women have particularly high rates of extragenital STIs, and performing only urine-based screening misses a majority of infections [Patton, et al. 2014; Pitasi, et al. 2019]. Three-site testing (genital, pharyngeal, and rectal) for gonococcal and chlamydial infections should be the default testing plan for MSM and transgender women unless such testing is declined due to lack of exposure at a site. A recent study reported high rates of extragenital gonococcal and chlamydial infections in transgender men attending STI clinics [Pitasi, et al. 2019]; therefore, risk for extragenital STIs should be considered in this population as well.

Because nucleic acid amplification testing (NAAT) has much higher sensitivity than culture, it is preferred for diagnosis of gonococcal or chlamydial infection. The U.S. Food and Drug Administration has approved diagnostic extragenital gonorrhea and chlamydia tests [FDA 2019b], which should make access to testing more readily available.

For cervical infections, vaginal swabs are preferred over urine-based testing because of higher sensitivity. For urethral infections, urine testing is preferred because of comfort. For transgender women who have a neovagina, data are lacking regarding optimal specimen type (neovaginal swab vs. urine-based testing). There are some reports of gonococcal infections detected via testing obtained from the neovagina [van der Sluis, et al. 2015]. Self-obtained swabs for vaginal, rectal, and pharyngeal specimen types have performed well in many studies and are preferred by many patients [Taylor, et al. 2013; Lunny, et al. 2015; Workowski, et al. 2015; Dize, et al. 2016].

#### → KEY POINTS

- STI testing at close intervals, including extragenital testing for gonorrhea and chlamydia, and prompt treatment of STIs are integral components of PrEP management.
- STI rates decline more rapidly as higher numbers of at-risk individuals initiate PrEP, with an even greater reduction in STIs the more frequently STI testing occurs, even in the event of a 40% to 80% decrease in condom use [Jenness, et al. 2017].
- Although discussion of condom use is an important part of prevention messaging, PrEP initiation and treatment should not be tied to condom use.
- Because the sensitivity and specificity of self-collected rectal, vaginal, and pharyngeal swabs are comparable to those collected by a clinician [Workowski, et al. 2015], self-collected swabs are reasonable alternatives for patients who may prefer these methods.

## Hepatitis C Screening

An increased risk for HCV acquisition has been noted in MSM using PrEP [Hoornenborg, et al. 2017a; Price, et al. 2019]. MSM with HIV [Fierer 2010; Bradshaw, et al. 2013; Fierer and Factor 2015] and to a lesser degree MSM without HIV [McFaul, et al. 2015] are at increased risk for acute HCV. A case-control study of MSM with HIV found that the presence of recent ulcerative STIs or risk behaviors, such as unprotected receptive anal intercourse, sharing of sex toys, unprotected fisting, injecting drugs, and sharing straws when snorting drugs, contributes to increased risk of HCV acquisition [Vanommerig, et al. 2015]. These may also be important risk factors in the general population. New elevations in liver enzymes can be a sign of acute HCV (see the NYSDOH guideline [Treatment of Chronic HCV With Direct-Acting Antivirals > Acute HCV Infection](#)).

## Pregnancy Screening and Management

Individuals of childbearing potential who are using PrEP and wish to avoid pregnancy should be offered contraception. TDF/FTC for PrEP does not affect levels of hormonal contraceptives. In individuals using PrEP, routine assessment for pregnancy risk and screening as appropriate decreases potential concerns associated with unplanned pregnancies. When pregnancy is identified, clinicians should provide counseling about the risks and benefits of continuing TDF/FTC for HIV prevention during pregnancy. HIV acquisition risk is higher in pregnancy and is at its highest in the late pregnancy and early postpartum periods [Thomson, et al. 2018], and PrEP should be recommended if risk of HIV exposure continues. Risk of perinatal transmission is also significantly higher during pregnancy and breastfeeding in the setting of acute seroconversion [Singh, et al. 2012; Drake, et al. 2014].

Available data suggest that use of TDF/FTC as PrEP does not increase the risk of birth defects (the use of antiretroviral medications during pregnancy is monitored through the *Antiretroviral Pregnancy Registry [APR]*). Conflicting results have been observed in studies of bone mineral density in infants born to women taking TDF as a component of antiretroviral therapy (ART) for HIV [Vigano, et al. 2011; Siberry, et al. 2015]. One study suggested up to a 15% decrease in bone mineral density in infants exposed to TDF in utero compared with infants who were not exposed to TDF [Siberry, et al. 2015], whereas another study found no association between in utero TDF exposure and infant bone mineral density [Vigano, et al. 2011]. In a study of pregnant women who did not have HIV in whom TDF was used as prophylaxis to prevent transmission of hepatitis B, there was no difference in bone mineral density at one year in TDF-exposed infants compared with infants not exposed to TDF in utero [Salvadori, et al. 2019].

Infant exposure to TDF/FTC through breast milk is much lower than TDF exposure that occurs in utero; evidence to date suggests that TDF is safe during breastfeeding [Ehrhardt, et al. 2015; Liotta, et al. 2016]. Longer-term follow-up studies of TDF-exposed infants are ongoing and will provide further information and guidance on the use of PrEP in this setting [Mugwanya, et al. 2016]. Although data on breastfeeding effects are limited, TDF/FTC is commonly prescribed as part of an ART regimen before, during, and after pregnancy, and the benefit of preventing HIV infection and subsequent perinatal transmission among individuals at increased risk outweighs the theoretical concerns associated with prescribing TDF/FTC as PrEP during breastfeeding.

Encourage pregnant individuals to inform their obstetric and pediatric care providers when they are using PrEP medications or any other prescription or over-the-counter medications.

There are insufficient data on the safety of TAF/FTC in pregnancy, and TAF/FTC has not been studied in those who engage in receptive vaginal sex.

### → KEY POINTS

- Pregnancy is *not* a contraindication to TDF/FTC as PrEP.
- The use of antiretroviral medications during pregnancy is monitored through the *Antiretroviral Pregnancy Registry (APR)*.
- Information regarding medications used during breastfeeding is available through the *LactMed* database.

Follow-up and monitoring of patients receiving PrEP includes services that are part of a comprehensive prevention plan: risk-reduction counseling; access to condoms and syringes; STI, mental health, and substance use screening; and referral for treatment when indicated.

- See *PrEP Management Checklist* in this guideline for a schedule of visits and follow-up assessments for individuals using PrEP.

## Discontinuing PrEP

### ☑ RECOMMENDATIONS: Discontinuing PrEP

- Clinicians should discontinue pre-exposure prophylaxis (PrEP) in any patient who:
  - Has a confirmed positive HIV test. (A1) In this case, the antiretroviral (ARV) regimen should be converted to a fully active antiretroviral therapy (ART) regimen. (A1)
    - See the NYSDOH guideline *When to Initiate ART, With Protocol for Rapid Initiation*.
  - Develops a confirmed calculated creatinine clearance (CrCl) <50 mL/min while taking tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP. (A2) Consider switching to tenofovir alafenamide/emtricitabine (TAF/FTC) for men who have sex with men and for transgender women if CrCl >30 mL/min. (A3) *See discussion in text below for strategies and options for patients with reduced renal function.*
  - Does not adhere to HIV testing requirements. (A3)
- Clinicians should closely monitor patients who have chronic hepatitis B virus for potential viral rebound when PrEP with TDF/FTC or TAF/FTC is discontinued and develop an alternative treatment plan if necessary. (A2)

The 2-drug PrEP regimens of TDF/FTC and TAF/FTC are not adequate as treatment for HIV. If HIV infection is confirmed, PrEP should immediately be converted to a fully suppressive HIV treatment regimen (see section on *Managing a Positive HIV Test Result*).

Renal function should be monitored as outlined in *Monitoring and Ongoing Laboratory Testing* in this guideline. If an increase in serum creatinine or a decrease in calculated CrCl is observed, evaluate potential causes other than TDF or TAF use, such as the use of nonsteroidal anti-inflammatory drugs, spurious elevations due to creatine supplementation, or recent heavy exercise leading to muscle breakdown, and repeat testing to confirm the finding prior to considering discontinuation. To avoid further toxicity, TDF/FTC as PrEP should be discontinued in patients who develop a confirmed CrCl <50 mL/min. Although TDF/FTC for treatment of HIV can be adjusted to every-other-day dosing in patients with a CrCl between 30 and 49 mL/min, this strategy has not been established for PrEP and should not be used. TAF/FTC is an option for MSM and transgender women with CrCl >30 mL/min. On-demand dosing of TDF/FTC can be considered for MSM with borderline renal function, to decrease drug exposure.

Because discontinuation of TDF/FTC or TAF/FTC in patients with chronic, active hepatitis B virus (HBV) can result in exacerbations of HBV [Chamorro, et al. 2005; Dore, et al. 2010; Buti, et al. 2015], an alternative treatment plan for these individuals is critical.

- For more information, see Centers for Disease Control and Prevention *Recommendations for Routine Testing and Follow-up for Chronic Hepatitis B Virus (HBV) Infection*.

### → KEY POINTS

- PrEP can be discontinued for those no longer at risk of HIV acquisition because they have eliminated the sex or drug use behaviors that put them at risk.
- If renal dysfunction develops while an individual is taking TDF/FTC or TAF/FTC for PrEP, address potential reversible causes prior to discontinuing PrEP.

# Managing a Positive HIV Test Result

## RECOMMENDATIONS

### Suspected Acute HIV

- For patients who present with any symptoms of acute retroviral illness and for whom acute HIV is suspected, clinicians should perform a plasma HIV RNA assay in conjunction with a laboratory-based 4th-generation HIV test. (A2)
- Clinicians should inform patients with suspected acute HIV about the increased risk of transmitting HIV during acute HIV infection. (A2)
- For patients who have a nonreactive HIV test result but have HIV RNA  $\geq 5,000$  copies/mL, a clinician can make a presumptive diagnosis of acute HIV, perform HIV genotype testing, and **initiate antiretroviral therapy (ART)** that will be active against virus with potential mutations for tenofovir and emtricitabine. (A2)
- For patients who have a nonreactive HIV test result but have detectable HIV RNA  $< 5,000$  copies/mL, clinicians should:
  - Perform repeat HIV RNA testing and repeat HIV diagnostic testing according to the Centers for Disease Control and Prevention (CDC) *Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens* to exclude a false-positive test result vs. a true-positive test result with a blunted viral response due to the presence of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide/emtricitabine (TAF/FTC). (A2)
  - Recommend initiation of an ART regimen that will be active against virus with potential mutations for tenofovir and FTC while a definitive diagnosis is sought,\* unless suspicion for acute HIV is low. (A2)

### Asymptomatic Patients With a Reactive HIV Screening Test Result

- For asymptomatic patients who have a reactive HIV test result while using pre-exposure prophylaxis (PrEP), clinicians should:
  - Ask about medication interruption of any duration and identify any access or adherence barriers. (A3)
  - Ask about potential risk exposures since the previous testing. (A\*)
  - Ask about signs and symptoms of acute HIV since the previous visit (see the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*). (A2)
  - Perform supplemental diagnostic testing as soon as possible according to the CDC *Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens*. (A1)
- If supplemental laboratory testing confirms HIV, clinicians should (A2):
  - Perform quantitative HIV RNA testing, if not already obtained as part of the diagnostic algorithm for suspected acute HIV, to measure viral load and perform genotypic resistance testing (see the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*).
  - Recommend immediate initiation of ART that will be active against virus with potential mutations for tenofovir and emtricitabine; adjustments to the initial ART regimen can be made if indicated once genotypic resistance test results are available or if the patient experiences side effects.\*

### Ambiguous Test Results

- The use of TDF/FTC or TAF/FTC as PrEP may alter viral load and immune response and cause ambiguous HIV test results using the current CDC HIV testing algorithm. In cases of ambiguous HIV test results, clinicians should consult with a care provider experienced in HIV and PrEP care\* for guidance on appropriate next steps. (A3)
- If presumptive HIV treatment is initiated, clinicians should initiate ART that will be active against virus with potential resistance mutations for tenofovir and emtricitabine. (A2)

\*To consult an expert, call the NYSDOH AI CEI line at 1-866-637-2342.

## Suspected Acute HIV

Vigilance for [signs and symptoms of potential HIV seroconversion](#) in patients receiving PrEP is crucial. TDF/FTC or TAF/FTC as PrEP is not adequate treatment for acute or chronic HIV, and continued use in the presence of HIV may lead to the emergence of viral resistance to these drugs. Because tenofovir and emtricitabine are important components of many HIV treatment regimens, constructing an effective ART regimen may be more difficult when viral resistance compromises the efficacy of either or both agents.

The mean time from HIV exposure to onset of symptoms is generally 2 to 4 weeks, with a range of 5 to 29 days; however, some cases are asymptomatic and some have presented with symptoms up to 3 months after exposure [Apoola, et al. 2002]. This time course may be prolonged in patients who acquire HIV while on PrEP, and symptoms of acute HIV infection may be blunted by TDF/FTC or TAF/FTC use. While patients are being evaluated for acute HIV, care providers should advise them to refrain from sexual activity or to use condoms to minimize the risk of transmitting HIV to a partner without HIV.

For patients who have a nonreactive HIV test result but have HIV RNA  $\geq 5,000$  copies/mL, a clinician can make a presumptive diagnosis of acute HIV, perform HIV genotype testing, and recommend immediate initiation of ART that will be active against virus with potential mutations for tenofovir and emtricitabine while awaiting genotype results. FTC-associated resistance due to emergence of M184V/I is much more common than the emergence of tenofovir-associated resistance mutations [Lehman, et al. 2015; Hare, et al. 2019].

For patients who have a nonreactive HIV test result but have detectable HIV RNA  $< 5,000$  copies/mL, clinicians should repeat HIV RNA testing and repeat HIV diagnostic testing according to the CDC [Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens](#) to exclude a false-positive test result versus a true-positive test result with a blunted viral response due to the presence of TDF/FTC or TAF/FTC. Unless suspicion for acute HIV is low, initiate ART that will be active against virus with potential mutations for tenofovir and emtricitabine while a definitive diagnosis is sought. There are no definitive protocols for specific antiretroviral medications to use in the case of suspected seroconversion while on PrEP. A reasonable option would be to continue TDF/FTC or TAF/FTC and add cobicistat-boosted darunavir (Prezcobix) with either dolutegravir (Tivicay) or raltegravir (Isentress) while awaiting HIV confirmation and subsequent HIV resistance testing.

## Asymptomatic Patients With a Reactive HIV Screening Test Result

HIV acquisition in patients who are fully adherent to PrEP is rare. If a patient on PrEP tests positive for HIV on routine screening, determine if there has been any medication interruption or decreased adherence. Patients who are fully adherent have a higher likelihood that a positive HIV test is a false-positive test result than those who are not. For individuals who report adherence gaps, gaps in medication access, or symptoms consistent with acute HIV in the period since last HIV testing, the concern for a true-positive test result is higher. There are no commercially available tests of TDF concentrations to confirm longer-term adherence in someone with possible seroconversion on PrEP. Hair samples and dried blood spots are utilized as tests in research only. Because false-positive 4th-generation HIV test results occur and there is risk of HIV exposure if PrEP is discontinued, it is recommended that PrEP not be discontinued. Clinicians should decide whether to continue PrEP or intensify to a full HIV treatment regimen (see above) while awaiting confirmatory test results, based on degree of suspicion for a false-positive versus a true-positive HIV test result.

### → KEY POINT

- Because false-positive 4th-generation HIV test results do occur and there is risk of HIV infection if PrEP is discontinued, clinicians will have to decide whether to continue the PrEP regimen or intensify to a full HIV treatment regimen while awaiting confirmatory test results, based on degree of suspicion for a false-positive versus a true-positive HIV test result.

If supplemental testing confirms HIV infection, perform quantitative HIV testing (if not already obtained), and genotypic resistance testing, and recommend immediate initiation of ART that will be active against virus with potential mutations for TDF/FTC or TAF/FTC, as discussed above.

## Ambiguous Test Results

### → KEY POINT

- Consult with an experienced HIV care provider to manage a positive or ambiguous HIV test result.

There have been a few reported cases of ambiguous HIV test results among individuals taking TDF/FTC as PrEP, following the CDC *Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens*. [Hoornenborg and de Bree 2017; Knox, et al. 2017; Markowitz, et al. 2017; Zucker J, et al. 2018]. In each case, an HIV screening antigen/antibody test was reactive, but supplemental testing (HIV 1/2 antibody differentiation, HIV viral load, and/or Western blot) was not consistently reactive or had a delayed time to reactivity. The same is likely to be true for individuals taking TAF/FTC. If this occurs, repeat testing in a few days may resolve ambiguity if the original results are due to early infection or technical issues. If ambiguity persists, the options are to continue PrEP versus intensify to a full HIV treatment regimen while waiting for additional testing to resolve the ambiguity (see above), or to discontinue PrEP and allow viral replication to occur and be measured if the patient does have HIV. However, discontinuing PrEP leaves an uninfected individual at risk, while a person who does have HIV will lose the theoretical virologic and immunologic benefits of treating HIV at such an early stage. Given the complexities of this issue, it is recommended that care providers consult with an HIV expert for guidance.

- See *A Strategy for PrEP Clinicians to Manage Ambiguous HIV Test Results During Follow-Up Visits* [Smith, et al. 2018], for a thorough review of this topic.

### → KEY POINTS: REPORTING

- Clinicians must report confirmed cases of HIV according to New York State Law; see NYSDOH *Provider Reporting & Partner Services*.
- Clinicians should offer assistance notifying partners or should refer patients to other sources for partner notification assistance.
  - See NYSDOH *Provider Reporting & Partner Services*.
  - See New York City (NYC) Health *Contact Notification Assistance Program (CNAP)*.
- **Reporting of suspected seroconversion:** Clinicians who manage the care of patients on PrEP are strongly encouraged to immediately report any cases of suspected PrEP/PEP breakthrough HIV infection as follows:
  - **NYC:** Report cases to the NYC Department of Health and Mental Hygiene immediately by calling 212-442-3388 and following the directions detailed in the attached Health Alert.
  - **Rest of state:** Report cases to NYSDOH by calling 518-474-4284 or using DOH-4189 and contacting the local Partner Services Program to discuss the case.
  - See *November 2016 NYSDOH/NYC Health Dear Colleague Letter*.

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# All Recommendations

## ☑ All RECOMMENDATIONS: PrEP to Prevent HIV and Promote Sexual Health

### Candidates for PrEP

- Clinicians should recommend pre-exposure prophylaxis (PrEP) for individuals, including adolescents,\* who do not have but are at increased risk of acquiring HIV. (A1)
- For patients who are completing a course of non-occupational post-exposure prophylaxis (nPEP) and remain at risk for HIV, clinicians should recommend initiation of PrEP immediately after completion of nPEP. (A3)
  - See the NYSDOH AI guideline *PEP for Non-Occupational Exposure to HIV (nPEP)*.

\*The U.S. Food and Drug Administration (FDA) approved the use of tenofovir disoproxil fumarate (TDF/FTC) as PrEP on May 15, 2018. On October 3, 2019, the FDA approved the use of tenofovir alafenamide/emtricitabine (TAF/FTC) as PrEP for cisgender MSM and transgender women, including adolescents, weighing  $\geq 35$  kg (~77 lb) at high risk of acquiring HIV.

### Contraindications to TDF/FTC and TAF/FTC as PrEP

- Pre-exposure prophylaxis (PrEP) is contraindicated in any individual with HIV; clinicians should not prescribe either tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide/emtricitabine (TAF/FTC) as PrEP for any person who has a documented HIV diagnosis; in such cases, a full therapeutic antiretroviral regimen is required. (A1)
  - See NYSDOH AI guideline *Selecting an Initial ART Regimen*.
- Clinicians should not prescribe TDF/FTC as PrEP for any individual with a confirmed creatinine clearance (CrCl)  $< 60$  mL/min; in such cases, TDF/FTC as PrEP is contraindicated. (A1)
- Clinicians should not prescribe TAF/FTC as PrEP for any individual with a confirmed CrCl  $< 30$  mL/min; in such cases, TAF/FTC as PrEP is contraindicated. (A1)

### Pre-Prescription Medical Evaluation and Laboratory Testing

- Before prescribing pre-exposure prophylaxis (PrEP), clinicians should perform a medical evaluation of the candidate that includes:
  - Assessment for symptoms or signs of acute HIV, including a febrile, flu-like, or mono-like illness in the previous 6 weeks. (A3)
  - Assessment to identify recent risk encounters ( $< 72$  hours) and the potential need for post-exposure prophylaxis (PEP) prior to PrEP. (A3)
  - Inquiry about the individual's reproductive plans. (A3)
  - Evaluation of concomitant medications to identify nephrotoxic drugs or drugs that have interactions with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide (TAF/FTC) as PrEP. (A3)
    - See NYSDOH AI guideline *ART Drug-Drug Interactions*.
  - Laboratory testing listed in *Table 2: Recommended Laboratory Tests to Be Obtained Before Prescribing PrEP* (see ratings in table).
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV > Acute Retroviral Syndrome*.
- Clinicians should prescribe PrEP only after obtaining a specimen for testing using a 4th-generation antigen/antibody (recommended) or 3rd-generation immunoglobulin M (IgM)/IgG antibody (alternative) HIV test and, when appropriate, an HIV viral load test\* within 1 week before planned PrEP initiation. (A3)
  - PrEP may be initiated while results of laboratory-based HIV diagnostic tests are pending unless the individual had a high-risk exposure within the previous 72 hours that requires PEP, has symptoms or signs of acute HIV, or has a history of renal disease or hepatitis B virus. (A2)
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV > Acute Retroviral Syndrome*.
  - Clinicians should assure HIV test results are available and acted upon within 7 days of initiation. (A3)
    - See NYSDOH AI guidelines *Diagnosis and Management of Acute HIV* and *HIV Testing*.

\*Indications for an HIV viral load test: Symptoms of acute HIV in the past 6 weeks or potential injection or sexual exposure in the past 4 weeks.

## **☑ All RECOMMENDATIONS: PrEP to Prevent HIV and Promote Sexual Health**

### **Prescribing PrEP**

- Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) is the preferred regimen for pre-exposure prophylaxis (PrEP). Clinicians should prescribe TDF 300 mg/FTC 200 mg once daily with or without food as PrEP. (A1)
  - Tenofovir alafenamide/emtricitabine (TAF/FTC) once daily is an option for prevention of HIV through sexual exposure in cisgender MSM and transgender women. TAF 25 mg/FTC 200 mg is not a recommended option for sexual exposure through receptive vaginal sex.
  - TAF/FTC as PrEP is preferred in cisgender MSM and transgender women who have preexisting renal disease or osteoporosis.
- If daily dosing is a barrier to adherence or if episodic dosing is preferred, clinicians should evaluate the appropriateness of on-demand dosing of TDF/FTC as PrEP. (A3)

### **Monitoring**

- Clinicians should perform routine monitoring of patients using pre-exposure prophylaxis (PrEP) according to the recommendations in *Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP* (see table for ratings).

### **HIV Testing**

- Clinicians should:
  - Obtain a 4th-generation (recommended) or 3rd-generation (alternative) laboratory-based HIV screening test before initiation of PrEP. (A\*)
  - Repeat HIV testing 1 month after initiation for those reporting a risk exposure in the 30 days prior to PrEP initiation. (A2<sup>†</sup>)
  - Perform HIV testing every 3 months while a patient is using PrEP. (A3)
- If a patient presents with symptoms or signs of a flu-like illness consistent with possible acute retroviral syndrome, clinicians should perform HIV testing immediately according to guidelines for the evaluation of acute HIV, including an HIV viral load test and a laboratory-based 4th-generation HIV test. (A2)
  - See *Managing a Positive HIV Test Result* in this guideline and the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*.

### **Renal Function Testing**

- At the following intervals, clinicians should perform renal function testing, including testing serum creatinine level and calculated creatinine clearance (CrCl) :
  - Before initiating PrEP with tenofovir disoproxil fumarate (TDF/FTC) or tenofovir alafenamide/emtricitabine TAF/FTC. (A\*)
  - At 3 months after initiation. (B3)
  - At least every 6 months for the duration of use of TDF/FTC or TAF/FTC as PrEP; more frequent screening may be required in patients at higher risk for renal disease. (A3)
- Clinicians should discontinue daily TDF/FTC as PrEP if a patient develops a confirmed calculated CrCl <50 mL/min and consider other alternative dosing and options; see discussion in text for strategies and options for patients with reduced renal function. (A3)
- Clinicians should perform urinalysis at baseline and annually, assessing for urine glucose and protein. (B3)

### **Sexually Transmitted Infection (STI) Screening**

- At every visit, a care team member should assess patients for signs and symptoms of STIs, including syphilis and gonococcal and chlamydial infections, as part of a sexual history and treat these infections empirically based on symptoms while results are pending. (A2<sup>†</sup>)
- Clinicians should perform ongoing testing for syphilis and gonococcal and chlamydial infections every 3 months at all sites of exposure, regardless of symptoms, as specified in *Table 3: Recommended Monitoring and Ongoing Laboratory Testing for Patients Taking TDF/FTC or TAF/FTC as PrEP*. (A2<sup>†</sup>)

**☑ All RECOMMENDATIONS: PrEP to Prevent HIV and Promote Sexual Health**

**Hepatitis C Virus (HCV) Screening**

- Clinicians should obtain at least annual HCV testing for at-risk patients using PrEP. (A3)

**Pregnancy Screening and Management**

- Clinicians should assess for possibility of pregnancy in individuals of childbearing potential at every visit. (A3)

**Discontinuing PrEP**

- Clinicians should discontinue pre-exposure prophylaxis (PrEP) in any patient who:
  - Has a confirmed positive HIV test. (A1) In this case, the antiretroviral (ARV) regimen should be converted to a fully active antiretroviral therapy (ART) regimen. (A1)
    - See the NYSDOH guideline *When to Initiate ART, With Protocol for Rapid Initiation*.
  - Develops a confirmed calculated creatinine clearance (CrCl) <50 mL/min while taking tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP. (A2) Consider switching to tenofovir alafenamide/emtricitabine (TAF/FTC) for men who have sex with men and for transgender women if CrCl >30 mL/min. (A3) *See discussion in text below for strategies and options for patients with reduced renal function.*
  - Does not adhere to HIV testing requirements. (A3)
- Clinicians should closely monitor patients who have chronic hepatitis B virus for potential viral rebound when PrEP with TDF/FTC or TAF/FTC is discontinued and develop an alternative treatment plan if necessary. (A2)

**Suspected Acute HIV**

- For patients who present with any symptoms of acute retroviral illness and for whom acute HIV is suspected, clinicians should perform a plasma HIV RNA assay in conjunction with a laboratory-based 4th-generation HIV test. (A2)
- Clinicians should inform patients with suspected acute HIV about the increased risk of transmitting HIV during acute HIV infection. (A2)
- For patients who have a nonreactive HIV test result but have HIV RNA ≥5,000 copies/mL, a clinician can make a presumptive diagnosis of acute HIV, perform HIV genotype testing, and **initiate antiretroviral therapy (ART)** that will be active against virus with potential mutations for tenofovir and emtricitabine. (A2)
- For patients who have a nonreactive HIV test result but have detectable HIV RNA <5,000 copies/mL, clinicians should:
  - Perform repeat HIV RNA testing and repeat HIV diagnostic testing according to the Centers for Disease Control and Prevention (CDC) *Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens* to exclude a false-positive test result vs. a true-positive test result with a blunted viral response due to the presence of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide/emtricitabine (TAF/FTC). (A2)
  - Recommend initiation of an ART regimen that will be active against virus with potential mutations for tenofovir and FTC while a definitive diagnosis is sought,\* unless suspicion for acute HIV is low. (A2)

**Asymptomatic Patients With a Reactive HIV Screening Test Result**

- For asymptomatic patients who have a reactive HIV test result while using pre-exposure prophylaxis (PrEP), clinicians should:
  - Ask about medication interruption of any duration and identify any access or adherence barriers. (A3)
  - Ask about potential risk exposures since the previous testing. (A\*)
  - Ask about signs and symptoms of acute HIV since the previous visit (see the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*). (A2)
  - Perform supplemental diagnostic testing as soon as possible according to the CDC *Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens*. (A1)
- If supplemental laboratory testing confirms HIV, clinicians should (A2):

**☑ All RECOMMENDATIONS: PrEP to Prevent HIV and Promote Sexual Health**

- Perform quantitative HIV RNA testing, if not already obtained as part of the diagnostic algorithm for suspected acute HIV, to measure viral load and perform genotypic resistance testing (see the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*).
- Recommend immediate initiation of ART that will be active against virus with potential mutations for tenofovir and emtricitabine; adjustments to the initial ART regimen can be made if indicated once genotypic resistance test results are available or if the patient experiences side effects.\*

**Ambiguous Test Results**

- The use of TDF/FTC or TAF/FTC as PrEP may alter viral load and immune response and cause ambiguous HIV test results using the current CDC HIV testing algorithm. In cases of ambiguous HIV test results, clinicians should consult with a care provider experienced in HIV and PrEP care\* for guidance on appropriate next steps. (A3)
- If presumptive HIV treatment is initiated, clinicians should initiate ART that will be active against virus with potential resistance mutations for tenofovir and emtricitabine. (A2)

\*To consult an expert, call the NYSDOH AI [CEI line](tel:1-866-637-2342) at 1-866-637-2342.

# All Good Practices

## → ALL GOOD PRACTICES: PrEP to Prevent HIV and Promote Sexual Health

### Pre-Prescription Counseling and Assessment

- Assess the patient’s health literacy and ensure that the purpose, benefits, and risks associated with PrEP are understood.
- Individualize the decision to initiate pre-exposure prophylaxis (PrEP) by weighing the benefit of reducing the person’s risk of acquiring HIV against the potential adverse effects of the medication.
- Make clear that PrEP efficacy is highly dependent on adherence; assess for readiness and willingness to adhere to PrEP and recommended follow-up care and assess for barriers to adherence.
- Obtain a thorough sexual history and drug use history, identify risk-taking behaviors, encourage other safer sex practices and, if applicable, safer drug injection techniques.
  - See the NYSDOH AI guidelines *Substance Use Screening and Risk Assessment in Adults* and *Harm Reduction Approach to Treatment of All Substance Use Disorders*.
  - See New York City Department of Health and Mental Hygiene *Making the Sexual History a Routine Part of Primary Care*.
  - See *GOALS: A New Framework for Sexual History Taking in Primary Care*.
- Ask whether the individual has a sex partner (or partners) with known HIV; if yes, ask if the partner’s viral load status is known.
- Discuss with patients in serodifferent partnerships the benefits and risks of relying on their partner’s undetectable viral load achieved with ART alone versus the addition of PrEP for preventing sexual transmission of HIV.
- Counsel serodifferent couples who are considering the use of PrEP during attempts to conceive about the utility, safety, and possible risks of the medication and about other approaches to safer conception.
- Perform a psychosocial assessment and refer for appropriate social and psychological support services, as indicated, to minimize HIV risk and support maintenance in care.

### Monitoring and Ongoing Laboratory Testing

- Upon initiation of PrEP, clinicians should instruct patients to notify their care provider immediately if they experience side effects.
- Within 2 weeks of PrEP initiation, a member of the care team should follow up to ensure the following:
  - The patient has filled the prescription for PrEP and understands how to take the medication.
  - Any problems with payment for PrEP are identified and solved.
  - Side effects, if any, are addressed and assistance with management is provided.
- At each visit, clinicians should:
  - Assess adherence and discuss strategies for maintaining adherence.
  - Discuss risk reduction in the context of the individual’s sexual health or injection drug use.
  - Offer condoms and, if appropriate, syringe access.
  - Inquire about side effects and offer advice for management if needed.
- Clinicians should follow the schedule of visits detailed in the *PrEP Management Checklist*.

### Adherence and Retention in Care

- Clinicians should:
  - Provide adherence counseling during every patient contact.
  - Partner with care providers within or outside of their organization to provide services, including subspecialty services, mental health and substance use treatment, case management, navigation and linkage services, housing assistance, and income/benefits assessments.
  - Explore and address potential barriers to ongoing use of and adherence to PrEP.
  - Make every effort to avoid discontinuing PrEP or withholding it from a patient at risk of acquiring HIV.

### Risk Reduction

- At every patient encounter, clinicians should offer female/receptive or male/insertive condoms to help decrease the patient’s risk of acquiring HIV and other sexually transmitted infections (STIs).
- For patients who inject drugs or misuse mood-altering drugs, clinicians should:
  - Refer for substance use treatment and mental health support as appropriate.

→ ALL GOOD PRACTICES: PrEP to Prevent HIV and Promote Sexual Health

- Prescribe clean syringes and needles or refer to needle-exchange programs as indicated. See NYSDOH *Expanded Syringe Access Program* and *Syringe Exchange Programs*.

## Appendices: PrEP Checklists

### Pre-Prescription Patient Evaluation Checklist

PrEP PRE-PRESCRIPTION PATIENT EVALUATION CHECKLIST From the New York State Department of Health AIDS Institute guideline <i>PrEP to Prevent HIV and Promote Sexual Health</i>
<p><input type="checkbox"/> <b>READINESS AND WILLINGNESS TO ADHERE TO PrEP</b></p> <ul style="list-style-type: none"> <li>• Assess health literacy and assure that the purpose, benefits, and risks associated with PrEP are understood.</li> <li>• Identify potential barriers to adherence.</li> </ul>
<p><input type="checkbox"/> <b>HIV STATUS OF PATIENT'S SEX PARTNER(S)</b></p> <ul style="list-style-type: none"> <li>• Does the patient have sex partners who are known to have HIV?</li> </ul> <p><i>If yes, ask about each partner:</i></p> <ul style="list-style-type: none"> <li>• Is the partner's viral load status known?</li> <li>• Provide information about U=U.</li> </ul>
<p><input type="checkbox"/> <b>POTENTIAL DRUG-DRUG INTERACTIONS</b></p> <ul style="list-style-type: none"> <li>• Take a thorough medication history that includes prescription drugs, over-the-counter drugs, and nonprescription therapies.</li> <li>• Identify nephrotoxic medications and the potential need for increased renal monitoring.</li> </ul>
<p><input type="checkbox"/> <b>SUBSTANCE USE AND MENTAL HEALTH STATUS [a]</b></p> <ul style="list-style-type: none"> <li>• Refer to the <i>Mental Health Screening</i> quick reference guide.</li> </ul>
<p><input type="checkbox"/> <b>PSYCHOSOCIAL STATUS</b></p> <ul style="list-style-type: none"> <li>• Perform a psychosocial assessment.</li> <li>• Refer for appropriate social and psychological support services as indicated.</li> </ul>
<p><input type="checkbox"/> <b>REPRODUCTIVE PLANS</b></p> <ul style="list-style-type: none"> <li>• Is the patient trying to conceive?</li> <li>• Is the patient currently using contraception? If not, is the patient interested in using hormonal contraception or another effective method of contraception in addition to condoms?</li> <li>• Is the patient or the patient's partner currently pregnant?</li> <li>• Is the patient currently breastfeeding?</li> <li>• If yes to any of the above, consult the recommendations and information in the guideline section <i>Pregnancy Screening and Management</i>.</li> </ul>
<p><input type="checkbox"/> <b>PrEP PAYMENT ASSISTANCE</b></p> <ul style="list-style-type: none"> <li>• Connect the individual to resources for assistance with payment, such as the <i>NYSDOH PrEP Assistance Program</i>.</li> <li>• Other resources can be found through <i>NYSDOH Payment Options for Pre-Exposure Prophylaxis (PrEP)</i>.</li> </ul>
<p>[a] Substance use, mental health disorders, and psychosocial challenges are not exclusionary criteria. Assessment allows the clinician to provide appropriate referrals and offer a tailored prevention plan. Substance use and mental health disorders may be barriers to adherence and cofactors for increased risk for HIV acquisition.</p>

## Pre-Prescription Patient Education Checklist

PrEP PRE-PRESCRIPTION PATIENT EDUCATION CHECKLIST From the New York State Department of Health AIDS Institute guideline <i>PrEP to Prevent HIV and Promote Sexual Health</i>
<p><b>☐ USE OF TDF/FTC AS PrEP</b></p> <ul style="list-style-type: none"> <li>▪ Dosing and need for adherence.</li> <li>▪ Time to protection is based on pharmacokinetic modeling studies and has not been clinically determined.</li> <li>▪ For rectal exposure, protection against HIV acquisition is achieved after 7 days of TDF/FTC daily dosing and possibly earlier.</li> <li>▪ For genital and blood exposure, protection against HIV acquisition is likely achieved after 7 days of TDF/FTC daily dosing, but optimal protection is achieved after 20 days of daily dosing.</li> <li>▪ Taking 2 pills of TDF/FTC as PrEP on the day of initiation will decrease the time needed to achieve protective drug levels for all sites of exposure.</li> </ul>
<p><b>☐ COMMON SIDE EFFECTS ASSOCIATED WITH TDF/FTC AND TAF/FTC</b></p> <ul style="list-style-type: none"> <li>▪ Predominantly diarrhea, headache, abdominal pain, and dizziness.</li> <li>▪ Side effects are usually mild, peak at 1 month, and resolve within 3 months.</li> </ul>
<p><b>☐ LONG-TERM SAFETY OF TDF/FTC AND TAF/FTC AS PrEP</b></p> <ul style="list-style-type: none"> <li>▪ Data suggest clinical safety of oral TDF/FTC and TAF/FTC in individuals without HIV. Although long-term safety has not been established in individuals without HIV, TDF/FTC has been used safely in thousands of individuals with HIV since 2004; 24-month follow-up data show clinical safety of oral TDF in men without HIV who have sex with men. TAF/FTC has been used safely in individuals with HIV since 2016.</li> </ul>
<p><b>☐ POSSIBLE SYMPTOMS OF AND RESPONSE TO SEROCONVERSION/ACUTE HIV</b></p> <ul style="list-style-type: none"> <li>▪ Contact healthcare provider if any of the following symptoms occur: fever, rash, joint pain, oral ulcers, fatigue, night sweats, sore throat, malaise, muscle pain, loss of appetite.</li> <li>▪ Importance of prompt treatment plan in the event of HIV seroconversion.</li> </ul>
<p><b>☐ CRITERIA FOR DISCONTINUING PrEP</b></p> <ul style="list-style-type: none"> <li>▪ Positive HIV test result. ART will be offered, and follow-up diagnostic and HIV genotypic resistance testing should be performed.</li> <li>▪ Development of renal disease; no data for adjusting TDF/FTC or TAF/FTC dosing in those with a decreased CrCl. <ul style="list-style-type: none"> <li>▪ Daily PrEP with TDF/FTC should be discontinued if CrCl &lt;50 mL/min.</li> <li>▪ TAF/FTC should be discontinued if CrCl &lt;30 mL/min.</li> </ul> </li> <li>▪ Does not adhere to HIV testing requirements.</li> </ul>
<p><b>☐ ADDED VALUE OF CONDOM USE</b></p> <ul style="list-style-type: none"> <li>▪ PrEP greatly reduces but may not eliminate HIV transmission risk and does not protect against STIs other than HIV or against pregnancy.</li> </ul>
<p><b>☐ USE OF PrEP DURING PREGNANCY</b></p> <ul style="list-style-type: none"> <li>▪ <b>Benefits:</b> Decreased risk of HIV acquisition in the pregnant individual, which increases in pregnancy; decreased perinatal transmission. Acute HIV during pregnancy is a significant risk factor for perinatal transmission.</li> <li>▪ <b>Potential toxicity:</b> Although available data suggest that TDF/FTC does not increase risk of birth defects, conflicting results have been observed in studies of BMD, ranging from no association to up to a 15% decrease in BMD in infants born to individuals receiving TDF, with limited data on long-term follow-up to determine the effect and longevity of this initial decrease in infant BMD. Data are insufficient to exclude the possibility of harm.</li> <li>▪ <b>Benefit vs. risk:</b> For individuals who become pregnant while using PrEP, continuation of PrEP during pregnancy is an individual decision based on whether ongoing or new risks for HIV acquisition are present during pregnancy.</li> <li>▪ There are insufficient data on the safety of TAF/FTC in pregnancy, and TAF/FTC has not been studied for those having vaginal receptive sex.</li> </ul>
<p><b>Abbreviations:</b> BMD, bone mineral density; CrCl, creatinine clearance; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.</p>

## PrEP Management Checklist

<b>PrEP MANAGEMENT CHECKLIST: PRE-PRESCRIPTION, FOLLOW-UP, AND MONITORING</b> From the New York State Department of Health AIDS Institute guideline <i>PrEP to Prevent HIV and Promote Sexual Health</i>	
<p><b>□ PRE-PRESCRIPTION</b></p> <ul style="list-style-type: none"> <li>• Discuss PrEP use; clarify any misconceptions.</li> <li>• Perform baseline laboratory testing:                             <ul style="list-style-type: none"> <li>• HIV test with 4th-generation test (preferred) or 3rd-generation test (alternative).</li> <li>• HIV RNA testing if indicated, i.e., high-risk exposure in the prior 4 weeks or symptoms of acute HIV in the prior 6 weeks.</li> <li>• Calculated CrCl.</li> <li>• For all MSM and transgender women, 3-site testing (genital, rectal, and pharyngeal) for gonorrhea and chlamydia regardless of sites of reported exposure.</li> <li>• Syphilis screening, according to the laboratory's testing algorithm.</li> <li>• Pregnancy test for individuals of childbearing potential.</li> <li>• HBV serologies (HBsAg, anti-HBs, and anti-HBc [IgG or total]).</li> <li>• HCV serology.</li> <li>• HAV serology.</li> <li>• Urinalysis.</li> <li>• Serum liver enzymes.</li> </ul> </li> </ul>	<p><b>□ AFTER OBTAINING HIV TEST</b></p> <ul style="list-style-type: none"> <li>• If history of HBV, renal disease, or recent symptoms of acute HIV, wait for HIV test results; otherwise, prescribe PrEP.</li> <li>• TDF/FTC is the preferred regimen.</li> <li>• TAF/FTC is an alternative regimen for cisgender MSM and transgender women when appropriate.</li> <li>• Daily dosing is preferred.</li> <li>• On-demand PrEP is an acceptable alternative for cisgender men who have sex with men.</li> <li>• Assure HIV test results are available and acted upon within 7 days of initiation.</li> <li>• Contact patient in 2 weeks to ensure:                             <ul style="list-style-type: none"> <li>• Patient has filled prescription and understands how to take the medication.</li> <li>• Problems with payment for PrEP are solved.</li> <li>• Any side effects are addressed.</li> </ul> </li> <li>• Instruct patient to report side effects immediately.</li> </ul>
<p><b>□ AT EVERY FOLLOW-UP VISIT:</b> (Note: The frequency of follow-up visits should be individualized. Stable individuals may need to be seen only 1 to 2 times per year, with laboratory testing performed in the interim.)</p> <ul style="list-style-type: none"> <li>• Assess adherence and discuss strategies for maintaining adherence; explore and address potential barriers to ongoing use of and adherence to PrEP.</li> <li>• Discuss risk reduction in the context of the individual's sexual health or injection drug use; offer condoms and, if appropriate, syringe access.</li> <li>• Assess for possibility of pregnancy and offer birth control and pregnancy testing when appropriate.</li> <li>• Inquire about side effects and offer advice for management if needed.</li> <li>• Partner with providers who can provide needed services, including subspecialty medical care, mental health and substance use treatment, case management, navigation and linkage services, housing assistance, and income/benefits assessments.</li> <li>• Make every effort to avoid discontinuing PrEP or withholding it from a patient at risk of acquiring HIV.</li> <li>• Ask about symptoms suggestive of STIs and test those at risk.</li> <li>• Screen for symptoms of acute HIV and test if indicated.</li> </ul>	
<p><b>□ TESTING: EVERY 3 MONTHS</b> (Note: An in-person visit is not required for laboratory testing.)</p> <ul style="list-style-type: none"> <li>• Test for HIV infection, using a 4th-generation test (preferred) or a 3rd-generation test (alternative).</li> <li>• Test for syphilis; may consider less frequent screening in those at lower risk.</li> <li>• Test for gonorrhea and chlamydia; may consider less frequent screening in those at lower risk.</li> <li>• Perform NAATs for gonococcal and chlamydial infections for all patients at all sites of reported exposure.</li> <li>• For all MSM and transgender women, routinely perform 3-site testing (genital, rectal, and pharyngeal) for gonorrhea and chlamydia regardless of sites of reported exposure, unless declined.</li> <li>• Obtain serum creatinine and calculated CrCl at 3 months after initiation of TDF/FTC as or TAF/FTC PrEP and every 6 months thereafter.                             <ul style="list-style-type: none"> <li>• There are no data for adjusting TDF/TAF dosing in those with CrCl &lt;50 mL/min; discontinue TDF if confirmed CrCl &lt;50 mL/min.; discontinue TAF if confirmed CrCl &lt;30 mL/min. (See <i>Renal Function Testing</i> in the full guideline.)</li> <li>• Consider more frequent screening in those at higher risk (e.g., age &gt;40 years) or who have comorbidities.</li> </ul> </li> </ul>	

**PrEP MANAGEMENT CHECKLIST: PRE-PRESCRIPTION, FOLLOW-UP, AND MONITORING, *Continued***  
From the New York State Department of Health AIDS Institute guideline *PrEP to Prevent HIV and Promote Sexual Health*

- EVERY 6 MONTHS** (Note: An in-person visit is not required for laboratory testing.)
- Obtain serum creatinine and calculated CrCl at 3 months after initiation of TDF/FTC or TAF/FTC as PrEP and every 6 months thereafter.

- ANNUALLY**
- Urinalysis.
  - HCV serology for those at risk; may obtain more frequently for those at higher risk.

**Abbreviations:** anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; CrCl, creatinine clearance; FTC, emtricitabine; HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; IgG, immunoglobulin G; MSM, men who have sex with men; NAAT, nucleic acid amplification test; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

## GOALS: A New Framework for Sexual History Taking in Primary Care

Developed by Sarit A. Golub, PhD, MPH, Hunter College and Graduate Center, City University of New York, in collaboration with the NYC Department of Health and Mental Hygiene, Bureau of HIV, July 2019

**BACKGROUND:** Sexual history taking can be an onerous and awkward task that does not always provide accurate or useful information for patient care. Standard risk assessment questions (e.g., *How many partners have you had sex with in the last 6 months?*; *How many times did you have receptive anal sex with a man when he did not use a condom?*) may be alienating to patients, discourage honest disclosure, and communicate that the number of partners or acts is the only component of sexual risk and health.

In contrast, the GOALS framework is designed to streamline sexual history conversations and elicit information most useful for identifying an appropriate clinical course of action.

The GOALS framework was developed in response to 4 key findings from the sexual health research literature:

1. Universal HIV/STI screening and biomedical prevention education is more beneficial and cost-effective than risk-based screening [Wimberly, et al. 2006; Hoots, et al. 2016; Owusu-Edusei, et al. 2016; Hull, et al. 2017; Lancki, et al. 2018].
2. Emphasizing benefits—rather than risks—is more successful in motivating patients toward prevention and care behavior [Weinstein and Klein 1995; Schuz, et al. 2013; Sheeran, et al. 2014].
3. Positive interactions with healthcare providers promote engagement in prevention and care [Bakken, et al. 2000; Alexander, et al. 2012; Flickinger, et al. 2013].
4. Patients want their healthcare providers to talk with them about sexual health [Marwick 1999; Ryan, et al. 2018].

Rather than seeing sexual history taking as a means to an end, the GOALS framework considers the sexual history taking process as an intervention that will:

- Increase rates of routine HIV/STI screening;
- Increase rates of universal biomedical prevention and contraceptive education;
- Increase patients' motivation for and commitment to sexual health behavior; and
- Enhance the patient-care provider relationship, making it a lever for sexual health specifically and overall health and wellness in general.

### THE GOALS FRAMEWORK INCLUDES 5 STEPS:

1. **Give a preamble that emphasizes sexual health.** The healthcare provider briefly introduces the sexual history in a way that de-emphasizes a focus on risk, normalizes sexuality as part of routine healthcare, and opens the door for the patient's questions.
2. **Offer opt-out HIV/STI testing and information.** The healthcare provider tells the patient that they test everyone for HIV and STIs, normalizing both testing and HIV and STI concerns.
3. **Ask an open-ended question.** The healthcare provider starts the sexual history taking with an open-ended question that allows them to identify the aspects of sexual health that are most important to the patient, while allowing them to hear (and then mirror) the language that the patient uses to describe their body, partner(s), and sexual behaviors.
4. **Listen for relevant information and fill in the blanks.** The healthcare provider asks more pointed questions to elicit information that might be needed for clinical decision-making (e.g., 3-site versus genital-only testing), but these questions are restricted to specific, necessary information. For instance, if a patient has already disclosed that he is a gay man with more than 1 partner, there is no need to ask about the total number of partners or their HIV status in order to recommend STI/HIV testing and PrEP education.
5. **Suggest a course of action.** Consistent with opt-out testing, the healthcare provider offers *all* patients HIV testing, 3-site STI testing, PrEP education, and contraceptive counseling, unless any of this testing is specifically contraindicated by the sexual history. Rather than focusing on any risk behaviors the patient may be engaging in, this step focuses specifically on the benefits of engaging in prevention behaviors, such as exerting greater control over one's sex life and sexual health and decreasing anxiety about potential transmission.

**RESOURCES FOR IMPLEMENTATION:**

- **Script, rationale, and goals:** *Box 1*, below, provides a suggested script for each step in the **GOALS** framework, along with the specific rationale for that step and the goal it is designed to accomplish.
- **The 5Ps model for sexual history-taking (CDC):** Note that the GOALS framework is not designed to completely replace the 5Ps model (partners, practices, protection from STI, past history of STI, prevention of pregnancy); instead, it provides a framework for identifying information related to the 5Ps that improves patient-care provider communication, reduces the likelihood of bias or missed opportunities, and enhances patients’ motivation for prevention and sexual health behavior.

**Box 1: GOALS Framework for the Sexual History**

Component	Suggested Script	Rationale and Goal Accomplished
Give a preamble that emphasizes sexual health.	<i>I'd like to talk with you for a couple of minutes about your <b>sexuality and sexual health</b>. I talk to all of my patients about sexual health, because it's such an <b>important part of overall health</b>. Some of my patients have <b>questions or concerns</b> about their sexual health, so I want to make sure I <b>understand what your questions or concerns might be and provide whatever information or other help you might need</b>.</i>	<ul style="list-style-type: none"> <li>• Focuses on sexual health, not risk.</li> <li>• Normalizes sexuality as part of health and healthcare.</li> <li>• Opens the door for the patient’s questions.</li> <li>• Clearly states a desire to understand and help.</li> </ul>
Offer opt-out HIV/STI testing and information.	<i>First, I like to test all my patients for HIV and other sexually transmitted infections. Do you have any concerns about that?</i>	<ul style="list-style-type: none"> <li>• Doesn’t commit to specific tests, but does normalize testing.</li> <li>• Sets up the idea that you will recommend some testing regardless of what the patient tells you.</li> <li>• Opens the door for the patient to talk about HIV or STIs as a concern.</li> </ul>
Ask an open-ended question.	<p>Pick <b>one</b> (or use an open-ended question that you prefer):</p> <ul style="list-style-type: none"> <li>• <i>Tell me about your sex life.</i></li> <li>• <i>What would you say are your biggest sexual health questions or concerns?</i></li> <li>• <i>How is your current sex life similar or different from what you think of as your ideal sex life?</i></li> </ul>	<ul style="list-style-type: none"> <li>• Puts the focus on the patient.</li> <li>• Lets you hear what the patient thinks is most important first.</li> <li>• Lets you hear the language the patient uses to talk about their body, partners, and sex.</li> </ul>
Listen for relevant information and probe to fill in the blanks.	<ul style="list-style-type: none"> <li>→ <i>Besides [partner(s) already disclosed], tell me about any other sexual partners.</i></li> <li>→ <i>How do you protect yourself against HIV and STIs?</i></li> <li>→ <i>How do you prevent pregnancy (unless you are trying to have a child)?</i></li> <li>→ <i>What would help you take (even) better care of your sexual health?</i></li> </ul>	<ul style="list-style-type: none"> <li>• Makes no assumption about monogamy or about gender of partners.</li> <li>• Avoids setting up a script for over-reporting condom use.</li> <li>• Can be asked of patients regardless of gender.</li> <li>• Increases motivation by asking the patient to identify strategies/ interventions.</li> </ul>
Suggest a course of action.	<ul style="list-style-type: none"> <li>→ <i>So, as I said before, I'd like to test you for [describe tests indicated by sexual history conversation].</i></li> <li>→ <i>I'd also like to give you information about PrEP/contraception/other referrals. I think it might be able to help you [focus on benefit].</i></li> </ul>	<ul style="list-style-type: none"> <li>• Allows you to tailor STI testing to the patient so they don’t feel targeted.</li> <li>• Shows that you keep your word.</li> <li>• Allows you to couch education or referral in terms of relevant benefits, tailored to the specific patient.</li> </ul>

## References for further reading:

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