



# CLINICAL GUIDELINES PROGRAM

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

## PrEP to Prevent HIV Acquisition

Medical Care Criteria Committee, October 2017

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# PrEP to Prevent HIV Acquisition

## Purpose of this Guideline

**Medical Care Criteria Committee, October 2017**

Implemented in April 2015, the New York State (NYS) Blueprint to End the AIDS Epidemic by 2020 presents the Ending the Epidemic Task Force's recommended strategies to reduce the number of annual new HIV infections to 750 by the year 2020. Toward that end, the NYS three-point plan calls for identifying individuals with undiagnosed HIV infection, linking and retaining them in care that includes fully suppressive antiretroviral therapy, and access to pre-exposure prophylaxis (PrEP) as a proven strategy to prevent HIV infection among individuals at high risk. By including access to PrEP as a major element of this initiative, NYS is emphasizing the safety and effectiveness of PrEP as a method to prevent HIV infection. The purpose of this guideline is to provide clinical practitioners throughout NYS with the recommendations needed to successfully start and manage patients on PrEP.

Randomized placebo-controlled trials have demonstrated the efficacy of PrEP for prevention of HIV transmission in men who have sex with men (MSM), transgender women, persons who inject drugs (PWID), and in men and women who engage in heterosexual sex. Tenofovir disoproxil fumarate + emtricitabine (TDF/FTC; brand name, Truvada) is approved by the U.S. Food and Drug Administration for use as PrEP as one part of a comprehensive HIV prevention strategy for individuals at high risk.

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. NYS also emphasizes the importance of prescribing PrEP in conjunction with counseling on safer sex and safer injection practices.

### KEY POINTS

- In New York State, use of TDF/FTC as PrEP is a central component of the standard of care for prevention of HIV acquisition in those at high risk.
- A comprehensive HIV prevention plan includes PrEP, along with safer sex and safe injection practices.
- The NYS Department of Health (NYSDOH) Clinical Education Initiative (CEI) and the NYSDOH AIDS Institute HIV Education and Training Program offer training in methods of motivational counseling and in prevention interventions, such as HIV/AIDS Prevention Project (formerly known as Diffusion of Effective Behavioral Interventions [DEBIs]).

Although the overall number of new HIV infections is decreasing in NYS, newly acquired infections are continuing to rise in some subpopulations, such as young MSM [NYSDOH 2016] and transgender women and men.\* New infections also continue to be disproportionately higher in communities of color. PrEP is an effective option to prevent HIV infection and to supplement behavior change in these high-risk populations.

The NYSDOH AIDS Institute recognizes that a comprehensive approach is necessary to ensure that patients who will most benefit from the use of PrEP have access to and are effectively managed on PrEP. Key populations that are at highest risk of HIV, including transgender women [Kuhns et al. 2016], MSM, PWID, and couples with one partner with HIV infection and one without (i.e., serodiscordant couples), should be prioritized for outreach and access to ensure that they are aware of PrEP and its benefits. PrEP is particularly useful when the partner with HIV infection is not virally suppressed or whose viral suppression is unknown. Awareness and acceptance of PrEP are suboptimal among a broad range of care providers and in communities at risk. More educational efforts must be made to address barriers to PrEP [King et al. 2014], especially in the highest risk communities, such as black MSM [Philbin et al. 2016]

## What's New in This Guideline

This new evidence-based, clinically-focused *guideline* for administration and management of PrEP for prevention of HIV infection replaces the now-archived *guidance* document titled *Guidance for the Use of Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Transmission*. Key changes are summarized below.

### New recommendations:

- For patients who are completing a course of non-occupational post-exposure prophylaxis (nPEP), clinicians should recommend initiation of PrEP immediately after completion of nPEP (see Candidates for PrEP).
- Clinicians should educate patients about the time required to achieve protective concentrations of TDF/FTC for PrEP: 7 days of daily dosing for receptive anal sex and 20 days of daily dosing for all other activities, including insertive anal sex, vaginal sex, and injection drug use (see Prescribing PrEP).
- Clinicians should test for sexually transmitted infections every 3 months as part of PrEP monitoring and ongoing laboratory testing (see Monitoring and Ongoing Lab Testing).

### Key additions:

- Updated information on the relationship between PrEP efficacy and adherence, including data that suggest that women require nearly 100% adherence to achieve protective levels of TDF/FTC for PrEP (see Prescribing PrEP).
- Updates to information on HIV acquisition in patients who are using PrEP and the need for clinical vigilance for signs and symptoms of seroconversion in patients taking TDF/FTC as PrEP (see HIV Acquisition While Using PrEP)

### SELECTED RESOURCES: NYSDOH

- Ending the AIDS Epidemic in New York State: [https://www.health.ny.gov/diseases/aids/ending\\_the\\_epidemic/](https://www.health.ny.gov/diseases/aids/ending_the_epidemic/)
- NYSDOH PrEP/PEP Voluntary Provider Directory: [https://www.health.ny.gov/diseases/aids/general/prep/provider\\_directory.htm](https://www.health.ny.gov/diseases/aids/general/prep/provider_directory.htm)
- PrEP Assistance Program (PrEP-AP) Participating Providers: [https://www.health.ny.gov/diseases/aids/general/prep/docs/prep-ap\\_directory.pdf](https://www.health.ny.gov/diseases/aids/general/prep/docs/prep-ap_directory.pdf)
- PrEP-AP: [https://www.health.ny.gov/diseases/aids/general/prep/prep-ap\\_consumer.htm](https://www.health.ny.gov/diseases/aids/general/prep/prep-ap_consumer.htm)
- Payment Options for PrEP: [https://www.health.ny.gov/diseases/aids/general/prep/docs/payment\\_options.pdf](https://www.health.ny.gov/diseases/aids/general/prep/docs/payment_options.pdf)
- HIV/AIDS Educational Materials for Consumers: <https://www.health.ny.gov/diseases/aids/general/publications/orderinginfo.htm>
- [prepforsex.org](http://prepforsex.org/): <http://prepforsex.org/>

## Guideline Development

This guideline was developed by the NYSDOH AIDS Institute (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 provided to people with HIV, hepatitis C virus, and sexually transmitted infections and to improve drug user health and LGBT health throughout the State of New York. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the Medical Care Criteria Committee (Adult HIV and related guidelines) 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 next page). If recommendations are based on expert opinion, the rationale for the opinion is included.

<b>Table 1. AIDS Institute HIV Clinical Guidelines Program Recommendations Rating Scheme</b>	
<b>Strength of Recommendation</b>	<b>Quality of Supporting Evidence</b>
A = Strong	1 = At least 1 randomized trial with clinical outcomes and/or validated laboratory endpoints
B = Moderate	2 = One or more well-designed, nonrandomized trial or observational cohort study with long-term clinical outcomes
C = Optional	3 = Expert opinion

## References

- Kuhns LM, Reisner SL, Mimiaga MJ, et al. Correlates of PrEP Indication in a Multi-Site Cohort of Young HIV-Uninfected Transgender Women. *AIDS Behav* 2016;20(7):1470-7. [PMID: 26336946]
- King HL, Keller SB, Giancola MA, et al. Pre-exposure prophylaxis accessibility research and evaluation (PrEPARE Study). *AIDS Behav* 2014;18(9):1722-5. [PMID: 25017425]
- New York State Department of Health. HIV Incidence Estimates, New York State, 2014. 2016 Sep 30. [https://www.health.ny.gov/diseases/aids/general/statistics/docs/hiv\\_incidence\\_2014-2016.pdf](https://www.health.ny.gov/diseases/aids/general/statistics/docs/hiv_incidence_2014-2016.pdf) [accessed 2017 Oct 24]
- Philbin MM, Parker CM, Parker RG, et al. The Promise of Pre-Exposure Prophylaxis for Black Men Who Have Sex with Men: An Ecological Approach to Attitudes, Beliefs, and Barriers. *AIDS Patient Care STDS* 2016;30(6):282-90. [PMID: 27220036]

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\* from preliminary impressions and results from focus groups with people of trans-masculine experience held July and September, 2015, New York City Department of Health and Mental Hygiene, Bureau of HIV/AIDS Prevention and Control

## PrEP Efficacy

### Medical Care Criteria Committee, October 2017

HIV prevention with PrEP is the use of antiretroviral (ARV) medications by non-infected individuals to reduce their risk of acquiring HIV infection. Tenofovir disoproxil fumarate (TDF) alone and the combination TDF + emtricitabine (TDF/FTC; brand name, Truvada) have been studied as PrEP in multiple randomized controlled and open-label trials in several populations, including MSM [Grant et al. 2010; McCormack et al. 2016], heterosexual serodiscordant couples [Baeten et al. 2012], heterosexual men and women [Thigpen et al. 2012; Van Damme et al. 2012; Marrazzo et al. 2015], transgender women [Grant et al. 2014], and PWID [Choopanya et al. 2013]. All of the trials found PrEP to be safe. Although TDF alone has been effective as PrEP in some populations, TDF/FTC is currently the only regimen approved by the U.S. Food and Drug Administration (FDA) for PrEP. A recent meta-analysis suggests >70% protection across all studies in which >70% adherence was reported [Fonner et al. 2016]. Although the FEM-PrEP [Van Damme et al. 2012] and VOICE [Marrazzo et al. 2015] trials did not demonstrate a benefit of PrEP for heterosexual women, analyses found that the lack of effect was associated with poor adherence to the daily PrEP regimen. Other studies have demonstrated PrEP to be effective for women [Baeten et al. 2012].

Studies of other ARVs for use as oral and topical PrEP, such as maraviroc, dapivirine, tenofovir alafenamide (TAF), and long-acting injectable preparations of rilpivirine [Clinical Trials Registry 2016a] and cabotegravir [Clinical Trials Registry 2016b], are underway.

Although TAF has been approved as a substitute for TDF as part of fixed-dose combinations for treatment of HIV, it has not been FDA-approved for use as PrEP. Data suggest that tenofovir levels in vaginal tissue after administration of TAF are lower than for TDF [Garrett et al. 2016]. Given this difference and other potential differences between TAF and TDF, TAF should not be used for PrEP until formal trials are completed, even in patients with renal insufficiency who may not use TDF.

There are 2 case reports of individuals who acquired drug-resistant HIV [Knox et al. 2016; NYC Health 2016] and 1 report of an individual who acquired wild-type virus while using PrEP [Hoorneborg et al. 2017]. In all 3 cases, the individuals were using TDF/FTC correctly. It is theorized that in the case of wild-type acquisition, despite good adherence, the potential exposure to HIV was very high given the number of condomless exposures over the 6-month period.

<b>Box 1: Summary of PrEP Benefits and Risks</b>	
<b>PrEP Benefits</b>	<b>PrEP Risks</b>
<ul style="list-style-type: none"> <li>▪ Highly effective in reducing risk of HIV acquisition when used as prescribed:               <ul style="list-style-type: none"> <li>▫ &gt;90% effective in reducing risk through sexual activity when blood levels show &gt;90% adherence [Grant et al. 2010]</li> <li>▫ &gt;70% effective in reducing risk through injection drug use when patients were observed taking their medication [Choopanya et al. 2013]</li> </ul> </li> <li>▪ Regimen is one tablet, once per day</li> <li>▪ TDF/FTC has a good safety profile in people who do not have HIV infection and have used PrEP for up to 3 years [Tetteh et al. 2017]</li> <li>▪ Minimal side effects, most of which resolve fairly quickly and/or can be managed [Tetteh et al. 2017]</li> <li>▪ Appears to be safe for use during attempts to conceive and during pregnancy [AIDSinfo 2016]</li> </ul>	<ul style="list-style-type: none"> <li>▪ Not safe for individuals with impaired kidney function [FDA 2016]</li> <li>▪ Requires 7 to 20 days of daily use to build protective blood levels [Marrazzo et al. 2014; Terrault et al. 2016; Johnson et al. 2012; Rodger et al. 2016; Bujan and Pasqueier 2016; Vernazza et al. 2011; Lampe et al. 2011; Chin et al. 2013; CDC 2017; Anderson et al. 2012; Hendrix et al. 2013; Patterson et al. 2011]</li> <li>▪ Protection may be reduced without adherence to daily medication regimen [Dimitrov et al. 2016]</li> <li>▪ No protection against sexually transmitted infections other than HIV</li> <li>▪ Potential for risk compensation (i.e., more condomless sex) [Kuhns et al. 2016; Carlo Hojilla et al. 2016; Golub 2014; Liu et al. 2013]</li> <li>▪ May be associated with reversible osteopenia in younger individuals [Havens et al. 2017]</li> <li>▪ Continued use after HIV infection is acquired may result in development of drug-resistant virus [Lehman et al. 2015]</li> <li>▪ Requires careful monitoring in patients with chronic hepatitis B virus (HBV); see Box 3, p. 13.</li> </ul>

## References

- AIDSinfo. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States: Nucleoside and Nucleotide Analogue Reverse Transcriptase Inhibitors. 2016 Jun 7. <https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/197/tenofovir-disoproxil-fumarate-viread-tdf> [accessed 2017 Oct 24]
- Anderson PL, Glidden DV, Liu A, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med* 2012;4(151):151ra25. [PMID: 22972843]
- Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med* 2012;367(5):399-410. [PMID: 22784037]
- Bujan L, Pasquier C. People living with HIV and procreation: 30 years of progress from prohibition to freedom? *Hum Reprod* 2016;31(5):918-25. [PMID: 26975324]
- Carlo Hojilla J, Koester KA, Cohen SE, et al. Sexual Behavior, Risk Compensation, and HIV Prevention Strategies Among Participants in the San Francisco PrEP Demonstration Project: A Qualitative Analysis of Counseling Notes. *AIDS Behav* 2016;20(7):1461-9. [PMID: 25835463]
- CDC. Sexually Transmitted Diseases Treatment Guidelines, 2015. 2017 Mar 27. <https://www.cdc.gov/std/treatment/> [accessed 2017 Oct 24]
- Chin T, Hicks C, Samsa G, et al. Diagnosing HIV infection in primary care settings: missed opportunities. *AIDS Patient Care STDS* 2013;27(7):392-7. [PMID: 23802143]
- Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2013;381(9883):2083-90. [PMID: 23769234]
- Clinical Trials Registry. Phase II Safety and Acceptability of an Investigational Injectable Product, TMC278LA, for Pre-Exposure Prophylaxis (TMC278LA). 2016a Feb. <https://clinicaltrials.gov/ct2/show/NCT02165202> [accessed 2017 Oct 24]
- Clinical Trials Registry. Study to Evaluate the Safety Tolerability and Acceptability of Long Acting Injections of the Human Immunodeficiency Virus (HIV) Integrase Inhibitor, GSK1265744, in HIV Uninfected Men (ECLAIR). 2016b Nov. <https://clinicaltrials.gov/ct2/show/NCT02076178> [accessed 2017 Mar 28]
- Dimitrov DT, Masse BR, Donnell D. PrEP Adherence Patterns Strongly Affect Individual HIV Risk and Observed Efficacy in Randomized Clinical Trials. *J Acquir Immune Defic Syndr* 2016;72(4):444-51. [PMID: 26990823]
- FDA. Truvada package insert. 2016 Mar. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/021752s047lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021752s047lbl.pdf) [accessed 2017 Oct 24]
- Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS* 2016;30(12):1973-83. [PMID: 27149090]
- Garrett KL, Cottrell ML, Prince HM, et al. Concentrations of TFV and TFVdp in Female Mucosal Tissues After a Single Dose of TAF. CROI; 2016 Feb 22-25; Boston, MA. <http://www.croiconference.org/sessions/concentrations-tfv-and-tfvdp-female-mucosal-tissues-after-single-dose-taf>
- Golub SA. Tensions between the epidemiology and psychology of HIV risk: implications for pre-exposure prophylaxis. *AIDS Behav* 2014;18(9):1686-93. [PMID: 24719201]
- Grant RM, Anderson PL, McMahan V, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014;14(9):820-9. [PMID: 25065857]
- Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363(27):2587-99. [PMID: 21091279]
- Havens PL, Stephensen CB, Van Loan MD, et al. Decline in Bone Mass With Tenofovir Disoproxil Fumarate/ Emtricitabine Is Associated With Hormonal Changes in the Absence of Renal Impairment When Used by HIV-Uninfected Adolescent Boys and Young Men for HIV Preexposure Prophylaxis. *Clin Infect Dis* 2017;64(3):317-25. [PMID: 28013265]
- Hendrix CW, Chen BA, Guddera V, et al. MTN-001: randomized pharmacokinetic cross-over study comparing tenofovir vaginal gel and oral tablets in vaginal tissue and other compartments. *PLoS One* 2013;8(1):e55013. [PMID: 23383037]

- Hoornenborg E, Prins M, Achterbergh RCA, et al. Acquisition of wild-type HIV-1 infection in a patient on pre-exposure prophylaxis with high intracellular concentrations of tenofovir diphosphate: a case report. *Lancet HIV* 2017;4(11):e522-e528. [PMID: 28919303]
- Johnson MO, Sevelius JM, Dilworth SE, et al. Preliminary support for the construct of health care empowerment in the context of treatment for human immunodeficiency virus. *Patient Prefer Adherence* 2012;6:395-404. [PMID: 22654510]
- Knox DC, Tan DH, Harrigan PR, et al. HIV-1 Infection With Multiclass Resistance Despite Preexposure Prophylaxis (PrEP). CROI; 2016 Feb 22-25; Boston, MA. <http://www.croiconference.org/sessions/hiv-1-infection-multiclass-resistance-despite-preexposure-prophylaxis-prep>
- Kuhns LM, Reisner SL, Mimiaga MJ, et al. Correlates of PrEP Indication in a Multi-Site Cohort of Young HIV-Uninfected Transgender Women. *AIDS Behav* 2016;20(7):1470-7. [PMID: 26336946]
- Lampe MA, Smith DK, Anderson GJ, et al. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol* 2011;204(6):488.e1-8. [PMID: 21457911]
- Lehman DA, Baeten JM, McCoy CO, et al. Risk of drug resistance among persons acquiring HIV within a randomized clinical trial of single- or dual-agent preexposure prophylaxis. *J Infect Dis* 2015;211(8):1211-8. [PMID: 25587020]
- Liu AY, Vittinghoff E, Chillag K, et al. Sexual risk behavior among HIV-uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States. *J Acquir Immune Defic Syndr* 2013;64(1):87-94. [PMID: 23481668]
- Marrazzo JM, del Rio C, Holtgrave DR, et al. HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society-USA Panel. *JAMA* 2014;312(4):390-409. [PMID: 25038358]
- Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. *N Engl J Med* 2015;372(6):509-18. [PMID: 25651245]
- McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* 2016;387(10013):53-60. [PMID: 26364263]
- NYC Health. 2016 DOHMH Health Alert #49: Potential Breakthrough HIV Infection in Patient on Pre-Exposure Prophylaxis. 2016 Oct 27. <https://www1.nyc.gov/assets/doh/downloads/pdf/hcp/han-PrEP-breakthrough.pdf> [accessed 2017 Oct 24]
- Patterson KB, Prince HA, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Sci Transl Med* 2011;3(112):112re4. [PMID: 22158861]
- Rodger AJ, Cambiano V, Bruun T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. *JAMA* 2016;316(2):171-81. [PMID: 27404185]
- Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016;63(1):261-83. [PMID: 26566064]
- Tetteh RA, Yankey BA, Nartey ET, et al. Pre-Exposure Prophylaxis for HIV Prevention: Safety Concerns. *Drug Saf* 2017;40(4):273-83. [PMID: 28130774]
- Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med* 2012;367(5):423-34. [PMID: 22784038]
- Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med* 2012;367(5):411-22. [PMID: 22784040]
- Vernazza PL, Graf I, Sonnenberg-Schwan U, et al. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *AIDS* 2011;25(16):2005-8. [PMID: 21716070]

## Candidates for PrEP

Medical Care Criteria Committee, October 2017

### ✓ RECOMMENDATIONS

#### Candidates for PrEP

- Clinicians should recommend PrEP for individuals, including adolescents\*, who do not have but are high risk of acquiring HIV and have adequate renal function. (A1)
  - HIV status should be confirmed by results of a negative 4th generation (recommended) or 3rd generation (alternative) HIV test within 1 week of planned PrEP initiation. (A3)
    - See Box 2. *Individuals to Whom Clinicians Should Offer PrEP and Contraindications to PrEP.*
- For patients who are completing a course of non-occupational post-exposure prophylaxis (nPEP), clinicians should recommend initiation of PrEP immediately after completion of nPEP. (A3)
  - See NYSDOH AI guideline *PEP for Non-Occupational Exposure to HIV (nPEP)*
- On May 15, 2018, the U.S. Food and Drug Administration (FDA) approved TDF/FCT (Truvada) use for adolescents weighing at least 35 kg (~77 lb) at high risk of acquiring HIV.

### 8→ KEY POINTS

- PrEP is an effective method for enhancing protection during periods when individuals, including adolescents, are at greatest risk of acquiring HIV.
- In New York State, use of TDF/FCT as PrEP is a central component and standard of care for prevention of HIV acquisition in those at high risk.
- As part of informed consent, clinicians should ensure that individuals understand that PrEP is not 100% effective in protecting against acquisition of HIV.
- Duration of use will depend on the length of time an individual remains at high risk for HIV infection (see Discontinuing PrEP for more information).
- The 2-drug PrEP regimen is not adequate as treatment for HIV infection and should be discontinued if HIV infection is confirmed.
- If HIV is diagnosed, antiretroviral therapy (ART) should be recommended for immediate initiation.
  - See NYSDOH AI guideline *When to Initiate ART*

PrEP should be prescribed for those at ongoing high risk of HIV acquisition, including adolescents, [Golden et al. 2016] as part of a comprehensive prevention plan [Buchbinder and Liu 2011]. A comprehensive plan will include counseling and education about adherence to PrEP [Blashill et al. 2015; Daughtridge et al. 2015; Marcus et al. 2014; Liu et al. 2014], ongoing monitoring with laboratory tests, education about risk reduction, and discussion of “risk compensation.” Increased risk-taking behaviors have been associated with PrEP use in some individuals, with a concomitant rise in other viral and bacterial sexually transmitted infections (STI) for which PrEP offers no protection [Kuhns et al. 2016; Carlo Hojilla et al. 2016; Golub 2014; Liu et al. 2013].

To establish that a patient is not HIV-infected, a screening test should be performed within 1 week of planned initiation of PrEP. The goals of ongoing, routine screening while PrEP is in use are to identify individuals with HIV infection as soon as possible to avoid continuation of the 2-drug PrEP regimen. Any HIV treatment regimen should contain at least 3 antiretrovirals that are active against HIV.

Patients who remain at high risk of 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 to Whom Clinicians Should Offer PrEP**

- Individuals, including adolescents, who engage in unprotected anal or vaginal intercourse with partners whose HIV status is unknown, have untreated HIV, or who do not have undetectable viral load while on treatment for HIV [Smith et al. 2012; Grov et al. 2013].
- Individuals who engage in unprotected anal or vaginal intercourse with partners who have HIV and undetectable viral load but wish to be on PrEP for additional protection (see the discussion of U=U, below).
- Women or men attempting to conceive with an HIV-infected partner.
- Women at ongoing risk of acquisition of HIV during pregnancy [Heffron et al. 2016]. Ongoing risk for serodiscordant couples during pregnancy includes inconsistent condom use, incomplete viral suppression in the partner with HIV infection, or both.
- Those who:
  - Have, or whose partners may have, multiple or anonymous sex partners.
  - Engage, or whose partners may engage, in sexual activity at sex parties or other high-risk venues.
  - Are involved, or whose partners may be involved, in transactional sex, such as sex for money, drugs, or housing, including commercial sex workers and their clients.
  - Have been diagnosed with at least one STI in the previous 12 months [Zetola et al. 2009; LaLota et al. 2011].
  - Report recreational use of mood-altering substances during sex, such as alcohol, methamphetamine [Smith et al. 2012; Grov et al. 2013; Buchacz et al. 2005; Zule et al. 2007; Koblin et al. 2011], cocaine, and ecstasy.
  - Report injecting substances, or have partners who inject substances, including illicit drugs and hormones.
  - Are receiving nPEP and demonstrate continued high-risk behavior or have used multiple courses of nPEP [Heuker et al. 2012]

Note: To identify MSM who are at higher risk of HIV acquisition, see HIV Incidence Risk Index (HIRI) for MSM (p. 12), a 7-item screening tool.

PrEP also may be appropriate for individuals who do not currently meet or acknowledge the risk criteria in Box 2, above. Such individuals include those who self-identify as at risk without disclosing any specific risk behaviors and individuals who acknowledge the possibility of or anticipate engaging in risk behaviors in the near future.

For individuals in a serodiscordant partnership, PrEP may be useful, even if the partner with HIV infection is receiving suppressive ART. Data from the Partners in Prevention HSV/HIV transmission study team [Donnell et al. 2010] and HPTN 052 [Cohen et al. 2011] demonstrated up to a 92% and 96% reduction, respectively, in HIV transmission risk in serodiscordant heterosexual couples when the partner with HIV infection was on suppressive ART. Full viral suppression is usually achieved 6 months after initiation of ART; until that time, transmission potential remains high [Mujugira et al. 2016]. In the Partners in Prevention demonstration project, use of PrEP as a “bridge” was highly effective in protecting the partner without HIV infection during the first 6 months that the partner with HIV infection received ART [Baeten et al. 2015]. In September of 2017 the NYSDOH endorsed the consensus statement from the Prevention Access Campaign that Undetectable = Untransmittable, or “U=U” [Zucker 2017; Prevention Access Campaign 2018]. Given these data, both members of a serodiscordant partnership should be active participants in the decision to initiate or discontinue PrEP. Couples may decide that antiretroviral treatment for the HIV-positive partner provides sufficient protection against HIV transmission. HIV-negative partners may choose to take PrEP, particularly if they have other sexual partners; are unsure of their partner’s viral load or their partner’s ability to stay consistently suppressed; or feel more secure in their sex lives with the added protection of PrEP.

Although the efficacy of PrEP during attempts to conceive has not been formally studied, it is an option for partners who do not have HIV infection. Evidence suggests that PrEP in this setting does not affect male fertility [Were et al. 2014] and is safe for women during the periconception period [Mugo et al. 2014]. However, more definitive research is needed.

**PrEP for adolescents:** To date, there are limited data on the efficacy and safety of PrEP use in individuals younger than 18 years of age, but safety studies in this population are underway [Hosek et al. 2016]. On May 15, 2018, the FDA approved use of TDF/FTC for PrEP in adolescents weighing at least 35 kg (~77 lb) [FDA 2018]. To date, there is no evidence of increased TDF/FTC toxicity in adolescents taking this combination as part of an ART regimen. Off-label use of TDF/FTC as part of a non-occupational post-exposure prophylaxis regimen is recommended for adolescents 13 to 18 years of age to prevent HIV infection after a high-risk exposure. The Centers for Disease Control and Prevention (CDC) and the International Antiviral Society–USA previously extended the indication for TDF/FTC to include PrEP for adolescents at high risk of HIV infection [CDC 2014; Marrazzo et al. 2014]. In addition to known concerns about renal complications associated with TDF use, concerns regarding osteopenia in younger age groups have been raised [Havens et al. 2017]. Bone density changes associated with TDF use are reversible upon discontinuation [Grant et al. 2016; Hightow–Weidman et al. 2016].

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 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 23 has long established the legal capacity of minors to consent to treatment and preventive services for sexually transmitted diseases (STDs). Provisions in Article 23 require that the Commissioner of Health promulgate a list of sexually transmitted diseases. A 2017 amendment to Article 23 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 23, 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.

#### References

- Baeten J, Heffron R, Kidoguchi L, et al. Near Elimination of HIV Transmission in a Demonstration Project of PrEP and ART. CROI; 2015 Feb 23–26; Seattle, WA. <http://www.croiconference.org/sessions/near-elimination-hiv-transmission-demonstration-project-prep-and-art>
- Blashill AJ, Ehlinger PP, Mayer KH, et al. Optimizing adherence to preexposure and postexposure prophylaxis: the need for an integrated biobehavioral approach. *Clin Infect Dis* 2015;60 Suppl 3:S187–90. [PMID: 25972502]
- Buchacz K, McFarland W, Kellogg TA, et al. Amphetamine use is associated with increased HIV incidence among men who have sex with men in San Francisco. *AIDS* 2005;19(13):1423–4. [PMID: 16103774]
- Buchbinder SP, Liu A. Pre-exposure prophylaxis and the promise of combination prevention approaches. *AIDS Behav* 2011;15 Suppl 1:S72–9. [PMID: 21331801]
- Carlo Hojilla J, Koester KA, Cohen SE, et al. Sexual Behavior, Risk Compensation, and HIV Prevention Strategies Among Participants in the San Francisco PrEP Demonstration Project: A Qualitative Analysis of Counseling Notes. *AIDS Behav* 2016;20(7):1461–9. [PMID: 25835463]
- CDC. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline. 2014. <https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf> [accessed 2017 Oct 24]
- Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011;365(6):493–505. [PMID: 21767103]
- Daughtridge GW, Conyngham SC, Ramirez N, et al. I Am Men's Health: Generating Adherence to HIV Pre-Exposure Prophylaxis (PrEP) in Young Men of Color Who Have Sex with Men. *J Int Assoc Provid AIDS Care* 2015;14(2):103–7. [PMID: 25331226]
- Donnell D, Baeten JM, Kiari J, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010;375(9731):2092–8. [PMID: 20537376]
- FDA. Supplement approval for Truvada. 2018 May 15. [https://www.accessdata.fda.gov/drugsatfda\\_docs/](https://www.accessdata.fda.gov/drugsatfda_docs/)

- appletter/2018/021752Orig1s055ltr.pdf [accessed 2018 May 17]
- Golden MR, Lindquist S, Dombrowski JC. Public Health–Seattle & King County and Washington State Department of Health Preexposure Prophylaxis Implementation Guidelines, 2015. *Sex Transm Dis* 2016;43(4):264–5. [PMID: 26967306]
- Golub SA. Tensions between the epidemiology and psychology of HIV risk: implications for pre-exposure prophylaxis. *AIDS Behav* 2014;18(9):1686–93. [PMID: 24719201]
- Grant R, Mulligan K, McMahan V, et al. Recovery of Bone Mineral Density After Stopping Oral HIV Preexposure Prophylaxis. CROI; 2016 Feb 22–25; Boston, MA. <http://www.croiconference.org/sessions/recovery-bone-mineral-density-after-stopping-oral-hiv-preexposure-prophylaxis>
- Grov C, Rendina HJ, Ventuneac A, et al. HIV risk in group sexual encounters: an event-level analysis from a national online survey of MSM in the U.S. *J Sex Med* 2013;10(9):2285–94. [PMID: 23809410]
- Havens PL, Stephensen CB, Van Loan MD, et al. Decline in Bone Mass With Tenofovir Disoproxil Fumarate/ Emtricitabine Is Associated With Hormonal Changes in the Absence of Renal Impairment When Used by HIV–Uninfected Adolescent Boys and Young Men for HIV Preexposure Prophylaxis. *Clin Infect Dis* 2017;64(3):317–25. [PMID: 28013265]
- Heffron R, Pintye J, Matthews LT, et al. PrEP as Peri-conception HIV Prevention for Women and Men. *Curr HIV/AIDS Rep* 2016;13(3):131–9. [PMID: 26993627]
- Heuker J, Sonder GJ, Stolte I, et al. High HIV incidence among MSM prescribed postexposure prophylaxis, 2000–2009: indications for ongoing sexual risk behaviour. *AIDS* 2012;26(4):505–12. [PMID: 22156963]
- Hightow–Weidman L, Magnus M, Beauchamp G, et al. Incidence and correlates of STIs among black men who have sex with men participating in a US PrEP study (THACO 105LB). 21st International AIDS Conference; 2016 Jul 18–22; Durban, South Africa. [http://www.aids2016.org/Portals/0/File/AIDS2016\\_Abstracts\\_LOW.pdf?ver=2016-08-10-154247-087](http://www.aids2016.org/Portals/0/File/AIDS2016_Abstracts_LOW.pdf?ver=2016-08-10-154247-087)
- Hosek S, Celum C, Wilson CM, et al. Preventing HIV among adolescents with oral PrEP: observations and challenges in the United States and South Africa. *J Int AIDS Soc* 2016;19(7(Suppl 6)):21107. [PMID: 27760684]
- Koblin BA, Mansergh G, Frye V, et al. Condom-use decision making in the context of hypothetical pre-exposure prophylaxis efficacy among substance-using men who have sex with men: Project MIX. *J Acquir Immune Defic Syndr* 2011;58(3):319–27. [PMID: 21765363]
- Kuhns LM, Reisner SL, Mimiaga MJ, et al. Correlates of PrEP Indication in a Multi-Site Cohort of Young HIV–Uninfected Transgender Women. *AIDS Behav* 2016;20(7):1470–7. [PMID: 26336946]
- LaLota M, Beck DW, Metsch LR, et al. HIV seropositivity and correlates of infection among heterosexually active adults in high-risk areas in South Florida. *AIDS Behav* 2011;15(6):1259–63. [PMID: 21153433]
- Liu AY, Hessol NA, Vittinghoff E, et al. Medication adherence among men who have sex with men at risk for HIV infection in the United States: implications for pre-exposure prophylaxis implementation. *AIDS Patient Care STDS* 2014;28(12):622–7. [PMID: 25396706]
- Liu AY, Vittinghoff E, Chillag K, et al. Sexual risk behavior among HIV–uninfected men who have sex with men participating in a tenofovir preexposure prophylaxis randomized trial in the United States. *J Acquir Immune Defic Syndr* 2013;64(1):87–94. [PMID: 23481668]
- Marcus JL, Buisker T, Horvath T, et al. Helping our patients take HIV pre-exposure prophylaxis (PrEP): a systematic review of adherence interventions. *HIV Med* 2014;15(7):385–95. [PMID: 24580813]
- Marrazzo JM, del Rio C, Holtgrave DR, et al. HIV prevention in clinical care settings: 2014 recommendations of the International Antiviral Society–USA Panel. *JAMA* 2014;312(4):390–409. [PMID: 25038358]
- Mugo NR, Hong T, Celum C, et al. Pregnancy incidence and outcomes among women receiving preexposure prophylaxis for HIV prevention: a randomized clinical trial. *JAMA* 2014;312(4):362–71. [PMID: 25038355]
- Mujugira A, Celum C, Coombs RW, et al. HIV Transmission Risk Persists During the First 6 Months of Antiretroviral Therapy. *J Acquir Immune Defic Syndr* 2016;72(5):579–84. [PMID: 27070123]
- Prevention Access Campaign. Risk of Sexual Transmission of HIV from a Person Living with HIV Who Has an Undetectable Viral Load. Messaging Primer & Consensus Statement. 2018 Jan 28. <https://www.preventionaccess.org/consensus> [accessed 2018 Mar 26]

- Smith DK, Pals SL, Herbst JH, et al. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2012;60(4):421-7. [PMID: 22487585]
- Were EO, Heffron R, Mugo NR, et al. Pre-exposure prophylaxis does not affect the fertility of HIV-1-uninfected men. *AIDS* 2014;28(13):1977-82. [PMID: 25259704]
- Zetola NM, Bernstein KT, Wong E, et al. Exploring the relationship between sexually transmitted diseases and HIV acquisition by using different study designs. *J Acquir Immune Defic Syndr* 2009;50(5):546-51. [PMID: 19367993]
- Zucker HA. Dear colleague letter. New York State Department of Health. 2017 Sep. [https://www.health.ny.gov/diseases/aids/ending\\_the\\_epidemic/docs/september\\_physician\\_letter.pdf](https://www.health.ny.gov/diseases/aids/ending_the_epidemic/docs/september_physician_letter.pdf) [accessed 2018 Mar 26]
- Zule WA, Costenbader EC, Meyer WJ, Jr., et al. Methamphetamine use and risky sexual behaviors during heterosexual encounters. *Sex Transm Dis* 2007;34(9):689-94. [PMID: 17471112]

## Screening Tool: HIV Incidence Risk Index (HIRI) for MSM

The following risk index (reprinted from Smith et al. 2012) was predictive of HIV seroconversion in two large prospective cohorts of MSM in the United States. The index can be used to prioritize patients for PrEP and other intensive HIV prevention efforts.

HIRI-MSM Risk Index*		
Question	Answer	Score
1. How old are you today (years)?	<18 years	0
	18 to 28 years	8
	29 to 40 years	5
	41 to 48 years	2
	≥49 years	0
2. How many men have you had sex with in the last 6 months?	>10 male sex partners	7
	6 to 10 male sex partners	4
	0 to 5 male sex partners	0
3. In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?	1 or more times	10
	0 times	0
4. How many of your male sex partners were HIV positive?	>1 positive partner	8
	1 positive partner	4
	<1 positive partner	0
5. In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	>5 times	6
	0 times	0
6. In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes	5
	No	0
7. In the last 6 months, have you used poppers (amyl nitrate)?	Yes	3
	No	0
<b>Total Score</b> (add down entries in right column to calculate total score <sup>§</sup> )		
<p>*To identify sexually active MSM in the practice, we recommend clinicians ask all their male patients a routine question: "In the past (time) have you had sex? (if yes), with men, women, or both?"</p> <p><sup>§</sup>If the score is 10 or greater, evaluate for PrEP or other intensive HIV prevention services. If the score is 9 or less, provide indicated standard HIV prevention services.</p>		

### Reference:

Smith DK, Pals SL, Herbst JH, et al. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. *J Acquir Immune Defic Syndr* 2012;60:421-427. [PMID: 22487585]

## Contraindications to PrEP

Medical Care Criteria Committee, October 2017

### ✓ RECOMMENDATION

#### Contraindications

- Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP is *contraindicated* for individuals:
  - With documented HIV infection. (AI)
  - With a creatinine clearance <60 mL/min. (AI)

The PrEP 2-drug regimen of TDF/FTC is not adequate for treating established HIV infection; therefore, it is contraindicated unless a patient tests HIV-negative within 1 week of proposed initiation. The combination pill used for PrEP includes TDF, which can cause renal toxicity and a reversible decrease in bone mineral density. TDF is contraindicated when used as PrEP for patients with a creatinine clearance <60 mL/min at the time of initiation [FDA 2016]. There is no role for adjusting TDF dosing in those with Cr Cl <60. Currently, there are no FDA-approved PrEP alternatives for people with eGFR<60; education regarding other prevention options, such as condom use and safer sex practices is essential.

Key components of patient education include a discussion of the risks of acquiring HIV, the importance of daily adherence, and, in turn, the risk of developing drug-resistant virus if adherence is poor [Dimitrov et al. 2016]. Alternative methods of HIV prevention may be best for those who report that they cannot adhere to a daily medication or who are unable to attend recommended monitoring visits for HIV testing and assessment for toxicities.

### 8 → KEY POINTS

- PrEP should not be withheld from people of any age group who are at risk of HIV acquisition.
- Education regarding the importance of, and strategies to support adherence may improve adherence to the daily PrEP regimen and recommended monitoring.
- For those who are unable to adhere to a daily medication regimen or recommended monitoring, alternative methods of HIV prevention should be explored and reinforced.

Care providers should carefully weigh the potential benefits and risks, including acquisition of HIV infection, before prescribing PrEP to a younger adolescent and should make clear that the efficacy of PrEP is highly dependent on daily adherence. The considerations outlined in Box 3, *Important Clinical Considerations When Prescribing PrEP*, below, are not absolute contraindications to prescribing PrEP. Clinicians should consider these factors and may proceed with caution.

### Box 3: Important Clinical Considerations When Prescribing PrEP

#### → If the patient has chronic active HBV infection:

- Both TDF and FTC are active against HBV infection.
  - For more information, see AASLD guidelines for treatment of chronic hepatitis B.
- If a patient is already taking tenofovir alafenamide (TAF) for HBV treatment, TAF should be switched to TDF/FTC for PrEP.
- Although not U.S. FDA-approved for the treatment of HBV, combination TDF/FTC may be used simultaneously as PrEP and as treatment for HBV infection.\*
- Continuation of TDF, TDF/FTC (or re-initiation of TAF, TAF/FTC) as HBV treatment should be recommended for patients who do not have HIV infection and for whom PrEP is no longer indicated.
- Discontinuation of TDF/FTC in patients with chronic HBV infection requires close monitoring for rebound HBV viremia.
- Individuals with chronic HBV infection who are not candidates for PrEP should be evaluated for treatment that follows published guidelines [Terrault et al. 2016]. Treatment regimens for HBV other than TDF/FTC are not protective against HIV acquisition.
  - For more information, see NYSDOH AI guideline *HBV-HIV Coinfection*

**Continued – Box 3: Important Clinical Considerations When Prescribing PrEP****→ 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.
- PrEP may be continued during pregnancy and breastfeeding if risk of HIV acquisition is ongoing.
- Suppressive ART (treatment as prevention) for the partner who has HIV infection is also essential to risk reduction.
- Prospectively report information regarding use of PrEP during pregnancy to the Antiretroviral Pregnancy Registry.

**→ If the patient is an adolescent:**

- PrEP may be appropriate for adolescents at risk of HIV acquisition.
- 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 (>65 years of age, black race, hypertension, or diabetes):**

- The greater possibility of kidney disease among individuals who have pre-existing risk factors will be an essential component of the risk-benefit discussion and shared decision-making regarding initiation of PrEP.
- Appropriate follow-up evaluations will be required for patients at risk of renal disease who elect to use PrEP with TDF/FTC.

**→ If the patient is taking other medications:**

- A thorough medication history that includes over-the-counter medications, such as nonsteroidal anti-inflammatory drugs, will reveal concomitant nephrotoxic drugs or drugs that have interactions with TDF/FTC.

**→ If the patient has osteopenia/osteomalacia/osteoporosis:**

- The risk of bone loss for individuals who have pre-existing risk factors or documented osteoporosis/osteomalacia/osteopenia is an essential component of the risk-benefit discussion and shared decision-making regarding initiation of PrEP.

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

**References**

- Dimitrov DT, Masse BR, Donnell D. PrEP Adherence Patterns Strongly Affect Individual HIV Risk and Observed Efficacy in Randomized Clinical Trials. *J Acquir Immune Defic Syndr* 2016;72(4):444-51. [PMID: 26990823]
- FDA. Truvada package insert. 2016 Mar. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/021752s047lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021752s047lbl.pdf) [accessed 2017 Oct 24]
- Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016;63(1):261-83. [PMID: 26566064]

# Pre-Prescription Counseling and Assessment

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Pre-PrEP Counseling and Assessment

- Clinicians should *not* withhold PrEP from candidates who:
  - Use other risk reduction practices inconsistently (A3)
  - Report substance use (A1)
  - Have mental health disorders (A3)
  - Report intimate partner violence (A3)
  - Have unstable housing or limited social support (A3).
- Clinicians should:
  - Assess the individual's health literacy and ensure that he or she understands the purpose, benefits, and risks associated with PrEP. (A3)
  - Individualize the decision to initiate PrEP by weighing the benefit of reducing a patient's personal risk of acquiring HIV infection against the potential adverse effects of the medication. (A3)
  - Make clear that PrEP efficacy is highly dependent on daily adherence; assess for readiness and willingness to adhere to PrEP and recommended follow-up care, and assess for barriers to adherence. (A3)
  - Ask whether the individual has a sex partner (or partners) with known HIV infection; if yes, ask if partner's viral load status is known. (B3)
  - Counsel serodiscordant couples who are considering using PrEP during attempts to conceive about the utility, safety, and possible risks of the medications and about other approaches to safer conception. (A3)
  - Obtain a thorough sexual history and drug use history, identify risk-taking behaviors, encourage safer sex practices, and, if applicable, safer drug injection techniques. (A2)
  - Perform a psychosocial assessment and refer for appropriate social and psychological support services, as indicated, to minimize HIV risk and support maintenance in care. (B3)
  - Perform substance use and mental health screenings. (A3)

## → RESOURCES: PREP PAYMENT ASSISTANCE

- For assistance with paying for PrEP, see:
  - NYSDOH: Payment Options for PrEP : [https://www.health.ny.gov/diseases/aids/general/prep/docs/payment\\_options.pdf](https://www.health.ny.gov/diseases/aids/general/prep/docs/payment_options.pdf)
  - PrEP-AP: <https://www.health.ny.gov/diseases/aids/general/resources/adap/prep.htm>

Patient education is critical to shared decision-making and to the success of PrEP as one part of a comprehensive HIV prevention plan. Clinicians should educate PrEP candidates about risks, benefits, and options and encourage discussion of the individual's preferences, needs, and circumstances. Medication adherence may be improved when patients participate in medication-related decisions [Johnson et al. 2012] and are informed about the strong efficacy of PrEP if taken as directed (see PrEP Follow-Up > Adherence and Retention in Care). Patient education provided in the individual's native or preferred language and tailored to the individual's level of comprehension will help to ensure that individuals understand the following:

- How PrEP works
- Benefits and risks of PrEP
- The need for strict adherence to maintain protective drug levels
- What PrEP will and will not do for them
- The need for ongoing use of safer sex and drug injection practices to avoid acquisition of drug-resistant HIV, other STIs, or pregnancy

**Health literacy:** A health literacy assessment should evaluate the individual's knowledge of the following

- Purpose of PrEP
- Importance of adherence to PrEP
- Importance of scheduled HIV testing and routine monitoring appointments
- Potential side effects of PrEP
- Process to obtain regular pharmacy refills for PrEP
- Methods for paying for PrEP and/or access to payment assistance for PrEP medications and related care services
  - See, for instance: Agency for Healthcare Research and Quality Health Literacy Measurement Tools, which are available in English and Spanish.

**Sex and drug use history:** As part of the HIV risk assessment, clinicians should have a detailed discussion with patients about sex and drug use history and risk-taking behaviors and should offer further counseling and referrals, such as for substance use counseling, as indicated. Clinicians should also help patients weigh the benefits of reducing the risk of HIV acquisition with the risks associated with starting PrEP, such as reduced renal function or bone loss.

Counseling should address the need for ongoing safer sex practices to further decrease the risk of HIV infection and to protect against other STIs. For PWID, safer injection techniques for protection against HIV and other blood-borne infections, such as hepatitis C virus (HCV) and HBV, should be discussed and/or implemented (such as HBV vaccination for those who are nonimmune).

- See NYSDOH Syringe Access and Disposal

**Status of sex partner(s) with HIV infection:** If an individual has a sex partner with known HIV infection, knowing the partner's treatment status and viral load can help inform the discussion of risk. HIV transmission is greatly reduced when a sex partner's HIV viral load is undetectable [Rodger et al. 2016]. If the patient's partner has detectable virus and genotypic information is unavailable, knowledge of the partner's treatment regimen may be useful. A partner with virus known to be resistant to the components of the PrEP regimen may pose a higher risk of transmission than one without resistance [Knox et al. 2016; NYC Health 2016].

**Psychosocial assessment:** The purpose of a psychosocial assessment is to determine the need for additional support for individuals who will receive PrEP and should address the following:

- Stability of housing and employment, need for government assistance, and level of education: For patients with unstable living situations, contact information, housing, and support network should be closely monitored.
- Support network: Does the patient have contact with family and friends?
- Safety: Is the patient afraid of a partner or of someone else close to him or her? If yes, refer to the New York State Office for the Prevention of Domestic Violence.

**Substance use and mental health screenings:** These screenings enable clinicians to identify modifiable barriers to adherence.

- See NYSDOH AI: Substance Use Screening (Quick Reference Guide)

Psychosocial challenges alone do not preclude the use of PrEP in a motivated patient willing to adhere to daily medication. Clinicians should address psychosocial and substance use challenges when they are identified by providing support and referrals for substance use treatment, mental health care, housing assistance, or protection from intimate partner violence.

#### → PrEP MANAGEMENT CHECKLISTS FOR CARE PROVIDERS

- PrEP Pre-Prescription Patient Evaluation Checklist, p. 18
- PrEP Pre-Prescription Patient Education Checklist, p. 19
- PrEP Management Checklist, p. 25

## References

- Johnson MO, Sevelius JM, Dilworth SE, et al. Preliminary support for the construct of health care empowerment in the context of treatment for human immunodeficiency virus. *Patient Prefer Adherence* 2012;6:395–404. [PMID: 22654510]
- Knox DC, Tan DH, Harrigan PR, et al. HIV-1 Infection With Multiclass Resistance Despite Preexposure Prophylaxis (PrEP). CROI; 2016 Feb 22–25; Boston, MA. <http://www.croiconference.org/sessions/hiv-1-infection-multiclass-resistance-despite-preexposure-prophylaxis-prep>
- NYC Health. 2016 DOHMH Health Alert #49: Potential Breakthrough HIV Infection in Patient on Pre-Exposure Prophylaxis. 2016 Oct 27. <https://www1.nyc.gov/assets/doh/downloads/pdf/hcp/han-PrEP-breakthrough.pdf> [accessed 2017 Oct 24]
- Rodger AJ, Cambiano V, Bruun T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. *JAMA* 2016;316(2):171–81. [PMID: 27404185]

# Pre-Prescription Patient Evaluation Checklist

Medical Care Criteria Committee, October 2017

<b>PrEP PRE-PRESCRIPTION EVALUATION CHECKLIST</b> From the New York State Department of Health AIDS Institute guideline <i>PrEP to Prevent HIV Acquisition</i> : <a href="http://www.hivguidelines.org">www.hivguidelines.org</a>
<p><input type="checkbox"/> <b>SYMPTOMS OF ACUTE HIV INFECTION</b></p> <ul style="list-style-type: none"> <li>▪ Has the patient experienced a febrile, “flu”-, “mono”-like illness in the previous 6 weeks?</li> <li>▪ Has the patient had a rash in the previous 6 weeks?</li> </ul> <p><i>If the answer to either question above is “yes,” then perform an HIV RNA test.</i></p>
<p><input type="checkbox"/> <b>READINESS AND WILLINGNESS TO ADHERE TO PrEP</b></p> <ul style="list-style-type: none"> <li>▪ Identify potential barriers to daily adherence.</li> <li>▪ Screen for health literacy.</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 infection?</li> </ul> <p><i>If yes, ask about each partner:</i></p> <ul style="list-style-type: none"> <li>▪ Is the partner taking antiretroviral therapy (ART)?</li> <li>▪ Is the partner’s HIV viral load suppressed? If no, is a resistance profile available?</li> </ul>
<p><input type="checkbox"/> <b>UNDERSTANDING OF PrEP</b></p> <ul style="list-style-type: none"> <li>▪ Ask “Why do you want PrEP?”</li> <li>▪ Ask: “What is your understanding of what PrEP will do for you?”</li> </ul>
<p><input type="checkbox"/> <b>POTENTIAL DRUG-DRUG INTERACTIONS</b></p> <ul style="list-style-type: none"> <li>▪ Ask the patient to list all drugs he or she is taking, including prescription drugs, over-the-counter drugs, and non-prescription therapies.</li> <li>▪ Identify nephrotoxic medications.</li> </ul>
<p><input type="checkbox"/> <b>SUBSTANCE USE AND MENTAL HEALTH STATUS*</b></p> <ul style="list-style-type: none"> <li>▪ Refer to the Substance Use Screening quick reference guide.</li> <li>▪ Refer to the Mental Health Screening quick reference guide.</li> </ul>
<p><input type="checkbox"/> <b>PSYCHOSOCIAL STATUS</b></p> <ul style="list-style-type: none"> <li>▪ Screen for intimate partner violence; see NYS Office for the Prevention of Domestic Violence.</li> <li>▪ Assess relationships and social support status.</li> <li>▪ Assess housing status/instability.</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 other 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 <i>Pregnancy Screening and Management</i> in this guideline</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 NYSDOH PrEP Assistance Program.</li> <li>▪ Other resources can be found through NYSDOH Payment Options for Pre-Exposure Prophylaxis (PrEP).</li> </ul>
<p>*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

Medical Care Criteria Committee, October 2017

<b>PrEP PRE-PRESCRIPTION EDUCATION CHECKLIST</b> From the New York State Department of Health AIDS Institute guideline on <i>PrEP to Prevent HIV Acquisition</i> : <a href="http://www.hivguidelines.org">www.hivguidelines.org</a>
<input type="checkbox"/> <b>USE OF PrEP</b> <ul style="list-style-type: none"> <li>▪ Dosing and need for daily adherence.</li> <li>▪ Number of sequential doses to achieve protective effect and differences in time to protection in men and women; available data suggest that it takes more time to accumulate protective drug concentrations in the female genital tract (20 days) than the rectum (7 days) [a].</li> </ul>
<input type="checkbox"/> <b>COMMON SIDE EFFECTS</b> <ul style="list-style-type: none"> <li>▪ Diarrhea, headache, abdominal pain, asthenia, and nausea.</li> <li>▪ Side effects are usually mild, peak at 1 month, and resolve within 3 months.</li> </ul>
<input type="checkbox"/> <b>LONG-TERM SAFETY OF PrEP [b]</b> <ul style="list-style-type: none"> <li>▪ 24-month follow-up data suggest clinical safety of oral tenofovir disoproxil fumarate (TDF) in individuals without HIV infection.</li> </ul>
<input type="checkbox"/> <b>POSSIBLE SYMPTOMS OF SEROCONVERSION/ACUTE HIV INFECTION</b> <ul style="list-style-type: none"> <li>▪ Contact healthcare provider if they experience any of the following symptoms: fever, rash, joint pain, oral ulcers (mouth sores), 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>
<input type="checkbox"/> <b>CRITERIA FOR DISCONTINUING PrEP</b> <ul style="list-style-type: none"> <li>▪ Positive HIV test result.               <ul style="list-style-type: none"> <li>▫ PrEP should be discontinued, antiretroviral therapy (ART) should be offered, and follow-up diagnostic and HIV genotypic resistance testing should be performed.</li> </ul> </li> <li>▪ Development of renal disease; there is no role for adjusting TDF dosing in those with Cr Cl &lt;60). It should be discontinued if Cr Cl is &lt;50.</li> <li>▪ Non-adherence to medication regimen or appointments.</li> <li>▪ Change in risk behaviors such that PrEP is no longer needed.</li> </ul>
<input type="checkbox"/> <b>ADDED VALUE OF CONDOM USE</b> <ul style="list-style-type: none"> <li>▪ PrEP greatly reduces but may not eliminate HIV transmission risk.</li> <li>▪ PrEP does not protect against other STIs or pregnancy.</li> </ul>
<input type="checkbox"/> <b>USE OF PrEP DURING PREGNANCY</b> <ul style="list-style-type: none"> <li>▪ <b>Benefit:</b> PrEP decreases the risk of acquiring acute HIV infection, which is a significant risk factor for mother-to-child transmission.</li> <li>▪ <b>Potential toxicity:</b> Although available data suggest that TDF/emtricitabine (FTC) does not increase risk of birth defects, up to a 15% decrease in bone mineral density (BMD) has been reported in infants born to women receiving TDF. Long-term follow-up data to determine the affect and longevity of this initial decrease in infant BMD are not yet available. Data are insufficient to exclude the possibility of harm [c].</li> <li>▪ <b>Benefit vs Risk:</b> For women who become pregnant while using PrEP, continuation of PrEP during pregnancy is an individualized decision based on whether ongoing or new risks for HIV acquisition are present during pregnancy.</li> </ul>
<p>a. Based on modeling, 7 days of daily dosing is needed to achieve protective concentrations for receptive anal sex and 20 days of daily dosing is needed for receptive vaginal sex.</p> <p>b. Although long-term safety has not been established in non-HIV-infected individuals, TDF/FTC has been used safely in thousands of individuals with HIV infection since 2004; 24-month follow-up data show clinical safety of oral TDF in men without HIV infection who have sex with men.</p> <p>c. TDF/FTC is a preferred component of ART during pregnancy.</p>

# Pre-Prescription Lab Testing

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Pre-Prescription Lab Testing

- Before prescribing PrEP, clinicians should perform a medical evaluation of the candidate that includes the following:
  - Laboratory testing listed in *Table 2: Recommended Laboratory Tests to be obtained before Prescribing PrEP*, below.
  - Assessment for symptoms or signs of acute HIV infection, including a febrile, “flu”-, or “mono”-like illness in the previous 6 weeks. (AII)
  - Evaluation of concomitant medications to identify nephrotoxic drugs or drugs that have interactions with the PrEP regimen. (AIII)
  - Inquiry about the individual’s reproductive plans. (AIII)
- Clinicians should prescribe PrEP only after receiving a negative 4th generation (recommended) or 3rd generation (alternative) HIV test within 1 week of planned PrEP initiation. (AIII)
- If the HIV test result is not available during the patient visit, the clinician should contact the patient to discuss the test result once it is available; if the result is negative, then the clinician should contact the patient’s pharmacy to prescribe PrEP. (AIII)
  - See NYSDOH AI guidelines *Diagnosis and Management of Acute HIV* and *HIV Testing*

All individuals who plan to start PrEP should have a confirmed negative HIV test within 1 week of PrEP initiation. If a confirmed negative result is not available at the time of the patient’s initial visit, the clinician should perform HIV testing. Once the results are available, and if they are negative, the patient should be informed, and the prescription provided to the pharmacy. If a patient tests positive for HIV infection, PrEP should not be prescribed, and the patient should be treated for HIV or referred for HIV care.

Table 2, Recommended Laboratory Tests to be Obtained before Prescribing 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, clinicians can use the opportunity to offer primary health care, and, as indicated, vaccinations for hepatitis A virus (HAV), HBV, human papillomavirus, meningococcus, and influenza.

For more information:

- See Centers for Disease Control and Prevention (CDC): Schedule for Immunizations for Adults Aged 19 Years or Older, 2017
- See NYSDOH: Health Advisory: NYSDOH Meningococcal Vaccine Recommendations for HIV-Infected Individuals and Those at High Risk of HIV Infection

## ➔ KEY POINT

- Initiation of PrEP in patients with undiagnosed HIV has led to development of drug-resistant virus [Lehman et al. 2015].

Clinicians should inquire about the individual’s reproductive plans and provide preconception counseling when indicated. Clinicians should 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 [Bujan and Pasquier 2016; Vernazza et al. 2011; Lampe et al. 2011] (see *Monitoring and Ongoing Lab Testing > Pregnancy Screening and Management*, p. 30).

<b>Table 2: Recommended Laboratory Tests to be Obtained before Prescribing PrEP</b>		
<b>Rating</b>	<b>Test</b>	<b>Comments</b>
AI	Baseline HIV test	<ul style="list-style-type: none"> <li>Obtain 4th generation (recommended) or 3rd generation (alternative) HIV screening test.*</li> </ul>
AI	HIV RNA testing	<ul style="list-style-type: none"> <li>Perform HIV RNA testing* in patients who:               <ul style="list-style-type: none"> <li>Have symptoms of acute HIV infection [Chin et al. 2013].</li> <li>Have a negative antibody test but report condomless anal or vaginal sex in the previous 4 weeks.</li> </ul> </li> </ul>
AI	Metabolic panel	<ul style="list-style-type: none"> <li>Obtain calculated creatinine clearance.               <ul style="list-style-type: none"> <li>Do not initiate PrEP in patients with a calculated creatinine clearance &lt;60 mL/min.</li> </ul> </li> </ul>
AI	Pregnancy test	<ul style="list-style-type: none"> <li>If a woman is pregnant when starting PrEP or becomes pregnant while using PrEP, discuss the known experience with the use of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for HIV treatment during pregnancy, benefits, and possible risks.</li> </ul>
AI	HBV serologies: HBsAg, anti-HBs, and anti-HBc (IgG or total)	<ul style="list-style-type: none"> <li>Vaccinate nonimmune patients (AII).</li> <li>Refer patients with chronic HBV for treatment.*</li> </ul>
AI	HAV serology	<ul style="list-style-type: none"> <li>Obtain for individuals at high risk for HAV infection, 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 abuse, or genetic liver diseases).</li> <li>Are travelers to countries with high or intermediate endemicity of infection.</li> <li>Use illicit drugs, and particularly injection drugs.</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 who are not otherwise required to receive HAV vaccination.</li> </ul> </li> <li>Individuals at risk of HAV-related morbidity or mortality.</li> <li>Vaccinate nonimmune patients.</li> </ul>
AII	Gonorrhea and chlamydia screening	<ul style="list-style-type: none"> <li>Perform nucleic acid amplification testing (NAAT) for gonococcal and chlamydial infection for all patients.</li> <li>Extragenital screening (rectal and pharyngeal) should be performed as appropriate for patients at high risk* [Golub et al. 2016].</li> <li>Self-collected vaginal and rectal swabs are reasonable options for patients who may prefer them over clinician-obtained swabs.</li> </ul>
AII	Syphilis screening	<ul style="list-style-type: none"> <li>Screen for syphilis according to the laboratory's testing algorithm.</li> <li>Clinicians should be aware of the syphilis screening algorithm used by their laboratory.*</li> </ul>
AIII	HCV serology	<ul style="list-style-type: none"> <li>Inform patients with HCV infection about the risk of transmission and offer treatment.</li> </ul>
Good practice (III)	Serum liver enzymes	<ul style="list-style-type: none"> <li>Increased serum liver enzymes may indicate acute or chronic viral hepatitis infection.</li> </ul>
Good practice (III)	Urinalysis	<ul style="list-style-type: none"> <li>As part of standard primary care, urinalysis is used to identify pre-existing renal disease, proteinuria, and/or glycosuria.</li> <li>Only calculated glomerular filtration rate (GFR) is used to guide decisions regarding prescribing or withholding PrEP according to renal function.</li> </ul>
<p>*For additional information, see the following:</p> <ul style="list-style-type: none"> <li>Related NYSDOH AI guidelines: <i>HIV Testing, Diagnosis and Management of Acute HIV</i>, and <i>HBV-HIV Coinfection</i>.</li> <li>CDC: 2015 Sexually Transmitted Diseases Treatment Guidelines.</li> </ul>		

## References

- Bujan L, Pasquier C. People living with HIV and procreation: 30 years of progress from prohibition to freedom? *Hum Reprod* 2016;31(5):918-25. [PMID: 26975324]
- Chin T, Hicks C, Samsa G, et al. Diagnosing HIV infection in primary care settings: missed opportunities. *AIDS Patient Care STDS* 2013;27(7):392-7. [PMID: 23802143]
- Golub SA, Pena S, Boonrai K, et al. STI Data From Community-Based PrEP Implementation Suggest Changes to CDC Guidelines. CROI; 2016 Feb 22-25; Boston, MA. <http://www.croiconference.org/sessions/sti-data-community-based-prep-implementation-suggest-changes-cdc-guidelines-0>
- Lampe MA, Smith DK, Anderson GJ, et al. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol* 2011;204(6):488.e1-8. [PMID: 21457911]
- Lehman DA, Baeten JM, McCoy CO, et al. Risk of drug resistance among persons acquiring HIV within a randomized clinical trial of single- or dual-agent preexposure prophylaxis. *J Infect Dis* 2015;211(8):1211-8. [PMID: 25587020]
- Vernazza PL, Graf I, Sonnenberg-Schwan U, et al. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *AIDS* 2011;25(16):2005-8. [PMID: 21716070]

# Prescribing PrEP

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Prescribing PrEP

- Clinicians should initially prescribe only a 30-day supply of PrEP.
  - At the 30-day follow-up visit, once adherence and tolerance is assessed a 60-day supply can be prescribed.
  - At the 3-month follow-up visit, and at 3-month intervals thereafter, a 90-day supply can be prescribed if adherence and tolerance remain stable and patients remain HIV uninfected.
    - See the PrEP Management Checklist for a schedule of visits and follow-up assessments in the first year of a patient's use of PrEP. (A3)

### Time to Protection

- Clinicians should educate patients about the time required to achieve protective concentrations of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for PrEP (A2):
  - 7 days of daily PrEP use for protection with receptive anal sex.
  - 20 days of daily PrEP use for protection with receptive vaginal sex, insertive anal or vaginal sex, and injection drug use.

**Prescribing TDF/FTC for PrEP:** The initial prescription for PrEP should be a 30-day supply without refills to ensure contact at the end of one month of treatment and the opportunity to assess for adherence and tolerance. For adults, the FDA-approved dosing for PrEP is tenofovir disoproxil fumarate 300 mg plus emtricitabine 200 mg (TDF 300 mg/FTC 200 mg fixed dose tablet; brand name, Truvada).

At the 30 day follow-up visit, if the patient has tolerated the medication and been successful with adherence, the clinician can elect to prescribe a 60-day supply. Thereafter, a regular schedule of 3-month follow-up visits can be established. At those visits, regular monitoring can be performed (see the PrEP Management Checklist for a schedule of visits and follow-up assessments for patient's using PrEP), and a 90-day supply of PrEP can be prescribed at each visit.

**Note:** TDF/FTC is dosed one pill daily with or without food.

## Time to Protection

Based on pharmacokinetic modeling, 7 days of daily dosing is needed to achieve protective concentrations of TDF/FTC for receptive anal sex, and 20 days of daily dosing is needed for all other activities, including insertive anal sex, vaginal sex, and injection drug use [Anderson et al. 2012; Hendrix et al. 2013; Patterson et al. 2011].

Intermittent PrEP is not recommended for anyone at this time. Although intermittent PrEP dosing remains an area of interest and is under active investigation, the complexity of the dosing schedule and the difficulties of using PrEP based on forecasted sexual activity make this strategy less optimal compared with daily dosing.

In men, the IPERGAY study, which evaluated intermittent pre- and post-exposure dosing of TDF/FTC, demonstrated an 86% relative risk reduction compared with placebo. However, the average number of pills taken per month by participants was 16, or approximately 4 pills per week, which is the level of adherence found to be the minimum necessary for protection in a study investigating daily dosing [Anderson et al. 2012]. The iPrEx-OLE study, an open-label extension of the iPrEx study [Grant et al. 2010], confirmed the finding that dosing of 4 or more pills per week offered protection for men enrolled in the study [Grant et al. 2014]. The HPTN 067 ADAPT study investigated daily versus time-driven versus event-driven dosing and found that adherence with

event-driven dosing was lower than daily dosing in the U.S. population of men and women studied. Women were most adherent to the daily dosing regimen. With intermittent dosing, protection remained optimal for MSM [Mannheimer et al. 2015]. Although intermittent PrEP use cannot be recommended, a modeling study of hypothetical risk of transmission in black MSM suggested that for either never or intermittent condom users, the addition of PrEP at even modest or high adherence could increase protection, and any PrEP use would increase protection for consistent condom users [Smith et al. 2015].

The effectiveness of intermittent PrEP in women has not been reported. In the HPTN 067 ADAPT study, levels of orally administered TDF have been found to be much lower in the vagina than in the anal compartment [Anderson et al. 2016]. Further data suggest that women require nearly 100% adherence to achieve protective levels [Cottrell et al. 2016]. Because of the differential pharmacokinetics in women taking TDF/FTC for PrEP, the use of intermittent PrEP cannot be recommended in this population.

#### KEY POINT

- **PrEP is not immediately protective.** Individuals who are using PrEP for HIV prevention must complete 7 to 20 days of daily use to achieve protective concentrations of TDF/FTC:
  - PrEP must be taken daily for 7 days to achieve protection against HIV acquisition through receptive anal sex.
  - PrEP must be taken daily for 20 days to achieve protection against HIV acquisition through other activities (vaginal sex, insertive anal sex, injection drug use).

#### References

- Anderson PL, Garcia-Lerma JG, Heneine W. Nondaily preexposure prophylaxis for HIV prevention. *Curr Opin HIV AIDS* 2016;11(1):94-101. [PMID: 26633641]
- Anderson PL, Glidden DV, Liu A, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med* 2012;4(151):151ra25. [PMID: 22972843]
- Cottrell ML, Yang KH, Prince HM, et al. A Translational Pharmacology Approach to Predicting Outcomes of Preexposure Prophylaxis Against HIV in Men and Women Using Tenofovir Disoproxil Fumarate With or Without Emtricitabine. *J Infect Dis* 2016;214(1):55-64. [PMID: 26917574]
- Grant RM, Anderson PL, McMahan V, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014;14(9):820-9. [PMID: 25065857]
- Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363(27):2587-99. [PMID: 21091279]
- Hendrix CW, Chen BA, Guddera V, et al. MTN-001: randomized pharmacokinetic cross-over study comparing tenofovir vaginal gel and oral tablets in vaginal tissue and other compartments. *PLoS One* 2013;8(1):e55013. [PMID: 23383037]
- Mannheimer S, Hirsch-Moverman Y, Loquere A, et al. HPTN 067/ADAPT study: a comparison of daily and intermittent pre-exposure prophylaxis (PrEP) dosing for HIV prevention in men who have sex with men and transgender women in New York City. MOACo305LB. 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention; 2015 Jul 19-22; Vancouver, Canada. [http://www.ias2015.org/WebContent/File/IAS\\_2015\\_\\_MED2.pdf](http://www.ias2015.org/WebContent/File/IAS_2015__MED2.pdf)
- Patterson KB, Prince HA, Kraft E, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. *Sci Transl Med* 2011;3(112):112re4. [PMID: 22158861]
- Smith DK, Herbst JH, Rose CE. Estimating HIV protective effects of method adherence with combinations of preexposure prophylaxis and condom use among African American men who have sex with men. *Sex Transm Dis* 2015;42(2):88-92. [PMID: 25585067]

# PrEP Management Checklist

Medical Care Criteria Committee, October 2017

<b>PrEP MANAGEMENT CHECKLIST: PRE-PRESCRIPTION, FOLLOW-UP, AND MONITORING</b> From the New York State Department of Health AIDS Institute guideline on <i>PrEP to Prevent HIV Acquisition</i> : <a href="http://www.hivguidelines.org">www.hivguidelines.org</a>	
<p><b><input type="checkbox"/> 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 HIV RNA testing if indicated)</li> <li>▫ Calculated creatinine clearance*</li> <li>▫ Pregnancy test for women of childbearing potential</li> <li>▫ HBV serologies (HBsAg, anti-HBs, and anti-HBc-IgG or total)</li> <li>▫ Urinalysis</li> <li>▫ HAV serology</li> <li>▫ STI screening (syphilis, gonorrhea, chlamydia)</li> <li>▫ HCV serology</li> <li>▫ Serum liver enzymes</li> </ul> </li> </ul>	<p><b><input type="checkbox"/> AFTER CONFIRMING NEGATIVE HIV TEST</b></p> <ul style="list-style-type: none"> <li>▪ Prescribe 30-day supply of PrEP.</li> <li>▪ Contact patient in 2 weeks to assess for side effects.</li> <li>▪ Instruct patient to report side effects immediately.</li> </ul>
<p><b><input type="checkbox"/> ALWAYS ENSURE ADHERENCE</b></p> <ul style="list-style-type: none"> <li>▪ Assess adherence and commitment at EVERY visit.</li> <li>▪ Schedule visits every 30 days for patients who report poor adherence or intermittent use of PrEP.</li> </ul>	
<p><b><input type="checkbox"/> 30-DAY FOLLOW-UP VISIT</b></p> <ul style="list-style-type: none"> <li>▪ Assess for side effects</li> <li>▪ Obtain serum creatinine and calculated creatinine clearance* for patients with borderline renal function or at increased risk for kidney disease (&gt;65 years of age, black race, hypertension, or diabetes).</li> <li>▪ Discuss risk reduction, provide condoms and, if applicable, provide syringes.</li> <li>▪ If adherence has been good, prescribe a 60-day refill.</li> <li>▪ Inform about need for 3-month visit for HIV test and follow-up (3 months after PrEP initiation).</li> </ul>	
<p><b><input type="checkbox"/> 3-MONTH VISIT</b></p> <ul style="list-style-type: none"> <li>▪ Perform HIV and syphilis tests; screen for gonorrhea and chlamydia.</li> <li>▪ Ask about symptoms suggestive of STIs and test those at high risk.</li> <li>▪ Screen for symptoms of acute HIV infection and test if indicated.</li> <li>▪ Perform pregnancy test for women of childbearing potential who are not using effective contraception or present with an STI.</li> <li>▪ Assess adherence; if adherence has been good provide a 90-day prescription.</li> <li>▪ Obtain serum creatinine and calculated creatinine clearance.*</li> <li>▪ Discuss risk reduction, provide condoms and, if applicable, provide syringes.</li> </ul>	
<p><b><input type="checkbox"/> 6-MONTH VISIT</b></p> <ul style="list-style-type: none"> <li>▪ Perform HIV and syphilis tests and screen for gonorrhea and chlamydia.</li> <li>▪ Ask about symptoms suggestive of STIs and test those at high risk.</li> <li>▪ Screen for symptoms of acute HIV infection and test if indicated.</li> <li>▪ Perform pregnancy test for women of childbearing potential who are not using effective contraception or present with an STI.</li> <li>▪ Perform STI screening tests.</li> <li>▪ Assess adherence; if adherence has been good provide a 90-day prescription.</li> <li>▪ Discuss risk reduction, provide condoms and, if applicable, provide syringes.</li> </ul>	

**Continued – PrEP MANAGEMENT CHECKLIST: PRE-PRESCRIPTION, FOLLOW-UP, AND MONITORING**

From the New York State Department of Health AIDS Institute guideline on *PrEP to Prevent HIV Acquisition*:  
[www.hivguidelines.org](http://www.hivguidelines.org)

**☐ 9-MONTH VISIT**

- Perform HIV and syphilis tests and screen for gonorrhea and chlamydia.
- Ask about symptoms suggestive of STIs and test those at high risk.
- Screen for symptoms of acute HIV infection and test if indicated.
- Perform pregnancy test for women of childbearing potential who are not using effective contraception or present with an STI.
- Obtain serum creatinine and calculated creatinine clearance.\*
- Assess adherence; if adherence has been good provide a 90-day prescription.
- Discuss risk reduction, provide condoms and, if applicable, provide syringes.

**☐ 12-MONTH VISIT**

- Perform HIV and syphilis tests and screen for gonorrhea and chlamydia.
- Perform urinalysis.
- Perform pregnancy test for women of childbearing potential who are not using effective contraception or present with an STI.
- Perform STI screening tests.
- Assess adherence; if adherence has been good provide a 90-day prescription.
- Discuss risk reduction, provide condoms and, if applicable, provide syringes.
- Obtain HCV serology and serum liver enzymes for MSM, PWIDs, and those with multiple sexual partners.

\*There is no role for adjusting TDF dosing in those with Cr Cl <60—discontinue if Cr Cl <50.

# PrEP Follow-Up

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Follow-Up

- Upon initiation of PrEP, clinicians should instruct patients to notify their care provider immediately if they experience side effects. (B3)
- Within 2 weeks of PrEP initiation, clinicians should follow up with the patient to: (B3)
  - Ensure the prescription was filled.
  - Troubleshoot problems with payment and connect the patient to resources for payment if needed.
  - Inquire about side effects and proper use of PrEP.
- At each visit, clinicians should: (B3)
  - Assess adherence and discuss strategies for maintaining adherence.
  - Discuss risk reduction in the context of the individual's sexual health and/or injection drug use needs.
  - Offer condoms, and, if appropriate, syringe access.
  - Manage side effects.

### Adherence and Retention in Care

- Clinicians should provide adherence counseling during every patient contact. (A3)

### Risk Reduction

- As an approach to decreasing acquisition of HIV and other STIs, clinicians should offer male and female condoms to all patients, including those using PrEP, at each visit. (A3)
- For patients who inject drugs, and others who misuse mood-altering drugs, clinicians should:
  - Make referrals for substance use treatment and mental health support as appropriate (A3)
  - Prescribe clean syringes and needles or refer to needle-exchange programs as indicated. (A2)
    - See NYSDOH: Expanded Syringe Access Program and Syringe Exchange Programs
- For patients in serodiscordant relationships, clinicians should discuss at each visit the benefits and risks of treatment as prevention (TasP) alone versus TasP + PrEP strategies for preventing transmission of HIV. (B3)

Possible side effects, such as diarrhea, headache, abdominal pain, weakness, and nausea, typically peak at 1 month and begin to improve, often resolving by 3 months on therapy [Glidden et al. 2016].

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

- See the PrEP Management Checklist (p. 25) for a schedule of visits and follow-up assessments in the first year of a patient's use of PrEP.

## Adherence and Retention in Care

In all studies of PrEP [Van Damme et al. 2012; Marrazzo et al. 2015; Fonner et al. 2016], efficacy is highly dependent on adherence. For patients who report intermittent use of PrEP, other strategies, including more frequent visits with medical and nonmedical providers, may be necessary to reinforce adherence. More frequent visits may also be necessary for adolescent patients to support adherence [Hosek et al. 2017]. Prescription of a limited 30-day supply and telephone contact or a visit for refills may be appropriate; however, a balance is necessary to ensure that patients do not run out of medication or use PrEP only intermittently during periods of high risk. Some providers use peer supporters or patient contracts to reinforce adherence to medication and appointments. Providers may contact the pharmacy to confirm that medication is being refilled at time intervals that are consistent with adherence (e.g., every 30 days if 30-day supply given). If patients are consistently unable to adhere to the regimen despite interventions to improve adherence, it may be appropriate to discuss discontinuing PrEP, and use tailored risk-reduction individualized to the patient.

PrEP should be viewed as 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 HPV vaccination for patients under 26 years of age and meningococcal vaccine when appropriate), linkage to specialty services, and other health maintenance activities. Clinicians should partner with 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. Referrals should also be made to support groups if indicated.

- For patient resources, see NYSDOH: HIV Patient Resources Directory.

## Risk Reduction

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

- For resources, see NYSDOH: PrEP and PEP.

If patients have partners with HIV infection, clinicians should emphasize the evidence that transmission risk is negligible if the individual with HIV infection in a serodiscordant partnership has a fully suppressed viral load [Rodger et al. 2016]. Clinicians may explore treatment barriers for a patient's partner.

## Side Effects

In clinical trials of treatment for HIV infection, the most common side effects of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) were mild and short-lived: diarrhea, headache, abdominal pain, weakness, and nausea. Gastrointestinal side effects can be alleviated with antidiarrheal agents, anti-gas medications, and antiemetics, as needed. Most side effects peak at 1 month and generally resolve within 3 months [Glidden et al. 2016]. Two weeks after initiation of PrEP, clinicians should follow up either in person or by telephone to assess side effects.

In the iPrEx [Grant et al. 2010, 2014] and Partners [Mujugira et al. 2016] PrEP trials, rash was not reported as a common side effect; therefore, development of a rash while on PrEP should prompt assessment for acute HIV infection [Apoola et al. 2002] and syphilis.

Renal impairment and bone density loss have been observed in patients taking TDF/FTC as treatment for HIV infection. Although renal dysfunction is uncommon, especially in younger patients on PrEP [Gandhi et al. 2016], regular laboratory monitoring for these parameters is necessary (see Table 3: Recommended PrEP Monitoring and Ongoing Laboratory Testing). If an increase in serum creatinine or a decrease in calculated creatinine clearance is observed, potential causes should be evaluated, and discontinuation or interruption of PrEP should be considered.

### KEY POINTS

- In clinical trials, rash was not a commonly observed side effect among participants taking PrEP [Grant et al. 2010, 2014; Mujugira et al. 2016].
- Rash can occur with secondary syphilis or acute HIV infection [Apoola et al. 2002] (see HIV Acquisition While Using PrEP, p. 36).

## References

- Abdul-Quader AS, Feelemyer J, Modi S, et al. Effectiveness of structural-level needle/syringe programs to reduce HCV and HIV infection among people who inject drugs: a systematic review. *AIDS Behav* 2013;17(9):2878-92. [PMID: 23975473]
- Apoola A, Ahmad S, Radcliffe K. Primary HIV infection. *Int J STD AIDS* 2002;13(2):71-8. [PMID: 11839160]
- Bramson H, Des Jarlais DC, Arasteh K, et al. State laws, syringe exchange, and HIV among persons who inject drugs in the United States: History and effectiveness. *J Public Health Policy* 2015;36(2):212-30. [PMID: 25590514]

- Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS* 2016;30(12):1973-83. [PMID: 27149090]
- Gandhi M, Glidden DV, Mayer K, et al. Association of age, baseline kidney function, and medication exposure with declines in creatinine clearance on pre-exposure prophylaxis: an observational cohort study. *Lancet HIV* 2016;3(11):e521-e28. [PMID: 27658870]
- Glidden DV, Amico KR, Liu AY, et al. Symptoms, Side Effects and Adherence in the iPrEx Open-Label Extension. *Clin Infect Dis* 2016;62(9):1172-7. [PMID: 26797207]
- Grant RM, Anderson PL, McMahan V, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014;14(9):820-9. [PMID: 25065857]
- Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363(27):2587-99. [PMID: 21091279]
- Hosek SG, Rudy B, Landovitz R, et al. An HIV Preexposure Prophylaxis Demonstration Project and Safety Study for Young MSM. *J Acquir Immune Defic Syndr* 2017;74(1):21-29. [PMID: 27632233]
- Jarlais DD. Systematic review research on needle/syringe programs and opiate substitution programs in low- and middle-income countries. *J Food Drug Anal* 2013;21(4):S59-S61. [PMID: 25267887]
- Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. *N Engl J Med* 2015;372(6):509-18. [PMID: 25651245]
- Mujugira A, Celum C, Coombs RW, et al. HIV Transmission Risk Persists During the First 6 Months of Antiretroviral Therapy. *J Acquir Immune Defic Syndr* 2016;72(5):579-84. [PMID: 27070123]
- Rodger AJ, Cambiano V, Bruun T, et al. Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. *JAMA* 2016;316(2):171-81. [PMID: 27404185]
- Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med* 2012;367(5):411-22. [PMID: 22784040]
- Van de Perre P, Jacobs D, Sprecher-Goldberger S. The latex condom, an efficient barrier against sexual transmission of AIDS-related viruses. *AIDS* 1987;1(1):49-52. [PMID: 3122790]

# Monitoring and Ongoing Lab Testing

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATION

### Monitoring

- Clinicians should perform routine monitoring of patients using PrEP according to the recommendations in Table 3, *Recommended PrEP Monitoring and Laboratory Testing*.

### HIV Testing

- Clinicians should obtain a 4th-generation (recommended) or 3rd-generation (alternative) laboratory-based HIV screening test before initiation of PrEP and every 3 months while a patient is using PrEP. (A3)
- Whenever patients present with symptoms or signs consistent with acute retroviral syndrome, clinicians should perform HIV testing immediately according to guidelines for the evaluation of acute HIV infection. (A2)
  - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV*
  - See *HIV Acquisition While Using PrEP* in this guideline

### Renal Function

- At the following intervals, clinicians should perform renal function testing, including creatinine, and calculated GFR: (B3)
  - Before initiating PrEP with TDF/FTC.
  - At 3 months after initiation.
  - At least every 6 months for the duration of PrEP.
- If the patient develops a calculated GFR  $\leq 50$  mL/min on PrEP with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), then PrEP should be discontinued. (A2)
- Clinicians should perform urinalysis at baseline and annually. (B3)

### HCV Screening

- Clinicians should obtain annual HCV screening for patients using PrEP. (A3)

### STI Screening

- Clinicians should assess patients for signs and symptoms of STIs, including syphilis and gonococcal and chlamydial infections, as part of a sexual history at every visit. (A3)
- Clinicians should perform ongoing screening for syphilis, gonococcal, and chlamydial infections as specified in Table 3: *Recommended PrEP Monitoring and Ongoing Laboratory Testing*.

### Pregnancy Screening and Management

- Clinicians should perform pregnancy testing in women of childbearing potential as follows (A3):
  - Every 3 months for women if effective contraception is not in use or whenever a new STI is diagnosed.
  - Annually when effective contraception is in use.
- Clinicians should counsel patients in serodiscordant relationships who are using PrEP and wish to conceive that the partner with HIV infection should achieve complete and sustained viral suppression for at least 6 months before attempts to conceive. (A2)

<b>Table 3: Recommended PrEP Monitoring and Ongoing Laboratory Testing</b>	
<i>Note: All recommended tests below are rated All unless indicated otherwise. Discussion follows table.</i>	
<b>Monitoring or Lab Test</b>	<b>Frequency</b>
HIV testing*: 4th generation (recommended) or 3rd generation assay (alternative) HIV screening test	Every 3 months
HIV serology screening test plus HIV RNA test*	When a patient has: <ul style="list-style-type: none"> <li>▪ Symptoms of acute HIV infection*</li> <li>▪ A negative antibody test but reports condomless anal or vaginal sex in the previous 4 weeks</li> </ul>
Serum creatinine and calculated creatinine clearance	3 months after initiation and every 6 months thereafter while on tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP
HCV serology*	Annually for those at risk
STI screening: <ul style="list-style-type: none"> <li>▪ Ask about STI symptoms</li> <li>▪ Screen for syphilis</li> <li>▪ Screen for gonococcal and chlamydial infection</li> <li>▪ Test and treat all symptomatic patients for STIs</li> </ul>	<ul style="list-style-type: none"> <li>▪ Ask about symptoms: Every visit</li> <li>▪ Screen for syphilis <ul style="list-style-type: none"> <li>▫ Every 3 months for MSM at high risk§ [Golub et al. 2016]</li> <li>▫ At least annually for individuals at lower risk</li> <li>▫ On-demand</li> </ul> </li> <li>▪ Clinicians should be aware of the syphilis screening algorithm used by their laboratory [CDC 2017]</li> <li>▪ Screen for gonorrhea and chlamydia <ul style="list-style-type: none"> <li>▫ Every 3 months in high risk§ individuals [Golub et al. 2016]</li> <li>▫ Annually for individuals at lower risk</li> <li>▫ On-demand</li> <li>▫ Extragenital screening (rectal, pharyngeal) should be performed for patients at high risk, including MSM and transgender women</li> <li>▫ Self-collected rectal and vaginal swabs are reasonable options for patients who may prefer them over clinician-obtained swabs</li> </ul> </li> </ul>
Pregnancy testing in women of childbearing potential	<ul style="list-style-type: none"> <li>▪ Every 3 months for women if effective contraception is not in use</li> <li>▪ Annually when effective contraception is in use</li> <li>▪ Whenever a new STI is diagnosed</li> </ul>
Urinalysis (BIII)	Annually
HCV RNA; HBV serology, if status is unknown; HBV DNA, if not immune; HAV serology, if unknown (Good practice III)	If a new elevation in serum liver enzymes is present
<p>*For additional information, see the following NYSDOH AI guidelines: <i>HIV Testing, Diagnosis and Management of Acute HIV</i>, and <i>HBV-HIV Coinfection</i>; CDC: 2015 Sexually Transmitted Diseases Treatment Guidelines.</p> <p>§Individuals at high risk of acquiring STIs include those who: self-identify and/or who report any of the following for self or partner: multiple or anonymous sex partners, bacterial STI diagnosed since last STI screening, participation in sex parties or sex in other high-risk venues, participation in any type of transactional sex, use of recreational substances during sex.</p>	

## HIV Testing

### KEY POINTS

- Routine HIV testing is an integral component of the safe use of PrEP.
- Frequent screening for HIV infection is performed to prevent development of drug-resistant virus and to protect against transmission of HIV.
- Evidence suggests that although rare, HIV genotypic resistance to PrEP can occur when PrEP is initiated during acute HIV infection and with breakthrough infections [Lehman et al. 2015].
- FTC has been associated with more frequently occurring resistance mutations than TDF [Lehman et al. 2015].

Extenuating circumstances may require the clinician to renew a prescription for PrEP pending a visit for HIV testing. If this occurs, the clinician may provide the patient with no more than a 1-month supply of PrEP, with no refills, and formulate a clear plan to document an HIV test within 1 week after the emergency refill.

If acute HIV infection 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. A 4th-generation HIV antigen/antibody combination test is the recommended serologic screening test. Detection of HIV RNA or antigen in the absence of serologic evidence of HIV infection 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 HIV Acquisition While Using PrEP, p. 36.

For more detailed recommendations on testing for acute HIV infection:

- See NYSDOH AI guidelines *Diagnosis and Management of Acute HIV* and *HIV Testing*

## Renal Function

A baseline urinalysis is important to identify pre-existing proteinuria before initiating PrEP. Also important is periodic monitoring while a patient is on PrEP. One sign of dose-dependent toxicity of TDF is the development of proteinuria. An elevated creatinine level should prompt a clinician to consider discontinuation of PrEP while further evaluation and repeat testing is performed.

Accumulating data suggest that more frequent creatinine screening may be appropriate in individuals >40 years of age [Gandhi et al. 2016]. Ongoing 3-month creatinine screening for these individuals or for patients with other comorbidities, such as diabetes or hypertension, or who are taking concomitant nephrotoxic drugs that might place them at higher risk for renal dysfunction may be appropriate.

## Hepatitis C Screening

An increased risk for HCV acquisition has been noted in at least one study of MSM using PrEP [Hoornenborg et al. 2017]. HIV-infected men who have sex with (MSM) [Bradshaw et al. 2013] and, to a lesser degree, HIV-uninfected MSM [McFaul et al. 2015] are at increased risk for acute HCV infection. A case control study in HIV-infected MSM has shown that the presence of recent ulcerative STIs and/or behaviors such as unprotected receptive anal intercourse, sharing sex toys, unprotected fisting, injecting drugs, and sharing straws when snorting drugs, contribute to increased risk of HCV acquisition [Vanhommerig et al. 2015]. These may also be important risk factors in the non-HIV-infected population. New elevations in liver enzymes can be a sign of acute HCV infection.

## STI Screening

### KEY POINT

- Because the sensitivity and specificity of self-collected rectal and vaginal swabs are comparable to those collected by a clinician [CDC 2017], self-collected swabs are reasonable alternatives for patients who may prefer these methods.

Most patients who elect to initiate PrEP are likely to be at high risk of acquisition of chlamydia, gonorrhea, and syphilis. Adults and adolescents at high risk should receive appropriate screening, including genital and extragenital testing (rectal, oropharyngeal), every 3 months as part of routine monitoring [Golub et al. 2016]. For those at lower risk, annual screening is indicated.

In one study, a subset of patients was asked about behavior change after 6 months of PrEP use: most had a similar number of partners as at baseline or initiation of PrEP, but 41% reported a decrease in condom use. In that study, 30% of PrEP users had been diagnosed with at least one STI within 6 months and 50% within 12 months [Volk et al. 2015]. Routine monitoring will allow for earlier diagnosis and treatment of STIs. Many STIs are asymptomatic, particularly gonococcal infections in women and pharyngitis and chlamydial infections in men and women; therefore, screening should not be based on the presence or absence of symptoms [CDC 2017]. Local data and data from other jurisdictions support testing for all STIs at every HIV testing visit to avoid late diagnoses of these infections [Golub et al. 2016; Liu et al. 2015].

## Pregnancy Screening and Management

In women using PrEP, routine pregnancy screening decreases potential concerns associated with unplanned pregnancies. When pregnancy is identified, clinicians should counsel women regarding the risks and benefits of continuing TDF/FTC for prevention during pregnancy.

Although available data suggest that use of PrEP with TDF/FTC does not increase the risk of birth defects, conflicting results have been obtained in studies of bone mineral density in infants born to women with HIV infection receiving TDF-containing ART regimens [Siberry et al. 2015; Vigano et al. 2011]. 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].

Infant exposure to TDF/FTC through breastmilk is much lower than are exposures that occur in utero; evidence to date suggests that TDF is safe during breastfeeding [Liota et al. 2016; Ehrhardt et al. 2015]. Longer-term follow-up studies of TDF-exposed infants are ongoing and will provide further information to guide clinicians and women on the use of PrEP in this setting [Mugwanya et al. 2016]. Although limited data on breastfeeding effects exist, 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 mother-to-child-transmission among women at high risk outweighs the theoretical concerns associated with prescribing TDF/FTC as PrEP during breastfeeding.

Clinicians should encourage pregnant women to inform their obstetrical and pediatric care providers when they are using PrEP medications, and/or any other prescription or over-the-counter medications.

### KEY POINTS

- 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.

## References

- Apoola A, Ahmad S, Radcliffe K. Primary HIV infection. *Int J STD AIDS* 2002;13(2):71-8. [PMID: 11839160]
- Bradshaw D, Matthews G, Danta M. Sexually transmitted hepatitis C infection: the new epidemic in MSM? *Curr Opin Infect Dis* 2013;26(1):66-72. [PMID: 23242342]
- CDC. Sexually Transmitted Diseases Treatment Guidelines, 2015. 2017 Mar 27. <https://www.cdc.gov/std/treatment/> [accessed 2017 Oct 24]
- Chin T, Hicks C, Samsa G, et al. Diagnosing HIV infection in primary care settings: missed opportunities. *AIDS Patient Care STDS* 2013;27(7):392-7. [PMID: 23802143]

- Ehrhardt S, Xie C, Guo N, et al. Breastfeeding while taking lamivudine or tenofovir disoproxil fumarate: a review of the evidence. *Clin Infect Dis* 2015;60(2):275–8. [PMID: 25313254]
- Gandhi M, Glidden DV, Mayer K, et al. Association of age, baseline kidney function, and medication exposure with declines in creatinine clearance on pre-exposure prophylaxis: an observational cohort study. *Lancet HIV* 2016;3(11):e521–e28. [PMID: 27658870]
- Golub SA, Pena S, Boonrai K, et al. STI Data From Community-Based PrEP Implementation Suggest Changes to CDC Guidelines. CROI; 2016 Feb 22–25; Boston, MA. <http://www.croiconference.org/sessions/sti-data-community-based-prep-implementation-suggest-changes-cdc-guidelines-0>
- Hoornenborg E, Achterbergh RCA, Schim Van Der Loeff MF, et al. Men who have sex with men starting pre-exposure prophylaxis (PrEP) are at risk of HCV infection: evidence from the Amsterdam PrEP study. *AIDS* 2017;31(11):1603–1610. [link]
- Lehman DA, Baeten JM, McCoy CO, et al. Risk of drug resistance among persons acquiring HIV within a randomized clinical trial of single- or dual-agent preexposure prophylaxis. *J Infect Dis* 2015;211(8):1211–8. [PMID: 25587020]
- Liotta G, Florida M, Andreotti M, et al. Growth indices in breastfed infants pre and postnatally exposed to tenofovir compared with tenofovir-unexposed infants. *AIDS* 2016;30(3):525–7. [PMID: 26765942]
- Liu A, Cohen S, Vittinghoff E, et al. Adherence, sexual behavior and HIV/STI incidence among men who have sex with men (MSM) and transgender women (TGW) in the US PrEP demonstration (Demo) project. TUACo202. 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention; 2015 Jul 19–22; Vancouver, Canada. [http://www.ias2015.org/WebContent/File/IAS\\_2015\\_\\_\\_MED2.pdf](http://www.ias2015.org/WebContent/File/IAS_2015___MED2.pdf)
- McFaul K, Maghlaoui A, Nzuruba M, et al. Acute hepatitis C infection in HIV-negative men who have sex with men. *J Viral Hepat* 2015;22(6):535–8. [PMID: 25412826]
- Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure Prophylaxis Use by Breastfeeding HIV-Uninfected Women: A Prospective Short-Term Study of Antiretroviral Excretion in Breast Milk and Infant Absorption. *PLoS Med* 2016;13(9):e1002132. [PMID: 27676257]
- Siberry GK, Jacobson DL, Kalkwarf HJ, et al. Lower Newborn Bone Mineral Content Associated With Maternal Use of Tenofovir Disoproxil Fumarate During Pregnancy. *Clin Infect Dis* 2015;61(6):996–1003. [PMID: 26060285]
- Vanhommerig JW, Lambers FA, Schinkel J, et al. Risk Factors for Sexual Transmission of Hepatitis C Virus Among Human Immunodeficiency Virus-Infected Men Who Have Sex With Men: A Case-Control Study. *Open Forum Infect Dis* 2015;2(3):ofv115. [PMID: 26634219]
- Vigano A, Mora S, Giacomet V, et al. In utero exposure to tenofovir disoproxil fumarate does not impair growth and bone health in HIV-uninfected children born to HIV-infected mothers. *Antivir Ther* 2011;16(8):1259–66. [PMID: 22155907]
- Volk JE, Marcus JL, Phengrasamy T, et al. No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting. *Clin Infect Dis* 2015;61(10):1601–3. [PMID: 26334052]

# Discontinuing PrEP

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Discontinuing PrEP

- Clinicians should discontinue PrEP in any patient who:
  - Has a confirmed positive HIV test. (A1)
  - Develops a calculated GFR  $\leq 50$  mL/min on PrEP with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). (A2)
  - Does not adhere to HIV testing requirements. (A3)
- Clinicians should closely monitor patients who have chronic HBV infection for potential rebound when PrEP with TDF/FTC is discontinued and develop an alternative treatment plan. (A2)
- PrEP should also 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 of acquiring HIV.

Patients who test positive for HIV while on PrEP should discontinue therapy immediately and be evaluated for acute HIV seroconversion and treatment of HIV.

Renal function should be monitored as outlined in Monitoring and Ongoing Lab Testing. To avoid further toxicity, PrEP should also be discontinued in patients who develop a GFR  $< 50$  mL/min. Although TDF/FTC for treatment of HIV can be adjusted to every-other-day dosing in patients with a GFR between 30 and 49 mL/min, this strategy has not been established for prophylaxis and should not be used.

Ongoing poor adherence to the PrEP medication regimen or with follow-up visits and HIV testing requires identification and discussion of any modifiable barriers, and of risks versus benefits of continuing with PrEP.

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

- For more information, see CDC: Recommendations for Routine Testing and Follow-up for Chronic HBV Infection.

### References

- Buti M, Casillas R, Riveiro-Barciela M, et al. Tenofovir discontinuation after long-term viral suppression in HBeAg negative chronic hepatitis B. Can HBsAg levels be useful? *J Clin Virol* 2015;68:61–8. [PMID: 26071338]
- Chamorro AJ, Casado JL, Bellido D, et al. Reactivation of hepatitis B in an HIV-infected patient with antibodies against hepatitis B core antigen as the only serological marker. *Eur J Clin Microbiol Infect Dis* 2005;24(7):492–4. [PMID: 15990987]
- Dore GJ, Soriano V, Rockstroh J, et al. Frequent hepatitis B virus rebound among HIV-hepatitis B virus-coinfected patients following antiretroviral therapy interruption. *AIDS* 2010;24(6):857–65. [PMID: 20216301]

# HIV Acquisition While Using PrEP

Medical Care Criteria Committee, October 2017

## ✓ RECOMMENDATIONS

### Suspected Acute HIV

- Clinicians should inform patients with suspected acute HIV infection about the increased risk of transmitting HIV during acute HIV infection (A2)

### Asymptomatic Patients

- For asymptomatic patients who receive a reactive HIV screening result while using PrEP, clinicians should:
  - Discontinue PrEP immediately; if supplemental laboratory testing does not confirm HIV infection, PrEP may be resumed. (A1)
  - In consultation with an experienced HIV care provider, recommend initiation of ART with at least 3 fully active antiretroviral medications. (A1)
  - Perform supplemental diagnostic testing according to the CDC HIV testing algorithm. (A1)
  - Ask about medication interruption of any duration and identify any access or adherence barriers. (A3)
- If supplemental laboratory testing confirms HIV infection, clinicians should:
  - Perform HIV RNA testing, if not already obtained as part of the diagnostic algorithm for suspected acute HIV infection, to measure viral load. (A2)
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV*
  - Perform HIV genotypic resistance testing. Adjustments to the initial ART regimen can be made once genotypic resistance results are available or when considering side effects. (A2)
    - See NYSDOH AI guideline *Selecting an Initial ART Regimen*

### Symptomatic Patients

- For patients who present with any symptoms of acute retroviral illness and for whom acute HIV infection is suspected, clinicians should perform a plasma HIV RNA assay in conjunction with an HIV screening test. (A2)
- The patient should continue PrEP until results are available, preferably within 1 week. (B3)
  - See NYSDOH AI guideline *HIV Testing*
- For patients who receive a nonreactive screening result with HIV RNA  $\geq 5,000$  copies/mL:
  - A clinician can make a presumptive diagnosis of HIV infection. (A2)
  - Recommend ART and perform HIV genotypic resistance testing; adjustments to the initial ART regimen can be made according to genotypic resistance results or side effects. (A2)
    - See NYSDOH AI guideline *Selecting an Initial ART Regimen*
- For patients who receive a nonreactive HIV screening result but have detectable HIV RNA with  $< 5,000$  copies/mL, repeat HIV RNA to exclude a false-positive result after discontinuation of PrEP; ART may be offered as described above for patients with a nonreactive screening result with HIV RNA  $\geq 5,000$  copies/mL while awaiting results from repeat HIV RNA testing. (A2)

Vigilance for signs and symptoms of potential HIV seroconversion in patients receiving PrEP is crucial. PrEP does not constitute adequate treatment for acute or chronic HIV infection, and continued therapy in the presence of HIV may lead to viral resistance to these drugs. Because tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) are important components of many HIV treatment regimens, construction of an effective ART regimen may be more difficult when viral resistance compromises the efficacy of either or both agents.

- For a list of signs and symptoms of acute seroconversion, see NYSDOH AI guideline *Diagnosis and Management of Acute HIV* > Presentation and Diagnosis > Acute Retroviral Syndrome.

The mean time from exposure to onset of symptoms is generally 2 to 4 weeks, with a range of 5 to 29 days; however, some cases have presented with symptoms up to 3 months after exposure [Apoola et al. 2002]. Theoretically, this time course may be prolonged in patients who become infected while on PrEP. While patients are being evaluated for acute HIV infection, they should refrain from sexual activity or should use condoms to minimize the risk of transmitting HIV to a partner without HIV infection. Patients who are confirmed negative for HIV after the recommended testing may resume PrEP.

#### 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:** Providers who manage 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 their local Partner Services Program to discuss the case.
    - See November 2016 NYSDOH/NYC Health Dear Colleague Letter

#### Reference

Apoola A, Ahmad S, Radcliffe K. Primary HIV infection. *Int J STD AIDS* 2002;13(2):71-8. [PMID: 11839160]

# All Recommendations

Medical Care Criteria Committee, October 2017

## ✓ ALL RECOMMENDATIONS

### Candidates for Prep

- Clinicians should recommend PrEP for individuals, including adolescents\*, who do not have but are high risk of acquiring HIV and have adequate renal function. (A1)
  - HIV status should be confirmed by results of a negative 4th generation (recommended) or 3rd generation (alternative) HIV test within 1 week of planned PrEP initiation. (A3)
    - See Box 2. Individuals to Whom Clinicians Should Offer PrEP and Contraindications to PrEP, p. 8.
- For patients who are completing a course of non-occupational post-exposure prophylaxis (nPEP), clinicians should recommend initiation of PrEP immediately after completion of nPEP. (A3)
  - See NYSDOH AI guideline *PEP for Non-Occupational Exposure to HIV (nPEP)*
- On May 15, 2018, the U.S. Food and Drug Administration (FDA) approved TDF/FTC (Truvada) use for adolescents weighing at least 35 kg (~77 lb) at high risk of acquiring HIV.

### Contraindications

- Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as PrEP is *contraindicated* for individuals:
  - With documented HIV infection. (A1)
  - With a creatinine clearance <60 mL/min. (A1)

### Pre-Prescription Counseling and Assessment

- Clinicians should not withhold PrEP from candidates who:
  - Use other risk reduction practices inconsistently (A3)
  - Report substance use (A1)
  - Have mental health disorders (A3)
  - Report intimate partner violence (A3)
  - Have unstable housing or limited social support (A3).
- Clinicians should:
  - Assess the individual's health literacy and ensure that he or she understands the purpose, benefits, and risks associated with PrEP. (A3)
  - Individualize the decision to initiate PrEP by weighing the benefit of reducing a patient's personal risk of acquiring HIV infection against the potential adverse effects of the medication. (A3)
  - Make clear that PrEP efficacy is highly dependent on daily adherence; assess for readiness and willingness to adhere to PrEP and recommended follow-up care, and assess for barriers to adherence. (A3)
  - Ask whether the individual has a sex partner (or partners) with known HIV infection; if yes, ask if partner's viral load status is known. (B3)
  - Counsel serodiscordant couples who are considering using PrEP during attempts to conceive about the utility, safety, and possible risks of the medications and about other approaches to safer conception. (A3)
  - Obtain a thorough sexual history and drug use history, identify risk-taking behaviors, encourage safer sex practices, and, if applicable, safer drug injection techniques. (A2)
  - Perform a psychosocial assessment and refer for appropriate social and psychological support services, as indicated, to minimize HIV risk and support maintenance in care. (B3)
  - Perform substance use and mental health screenings. (A3)

*Continued next page*

## ✓ ALL RECOMMENDATIONS – CONTINUED

### Pre-Prescription Lab Testing

- Before prescribing PrEP, clinicians should perform a medical evaluation of the candidate that includes the following:
  - Laboratory testing listed in *Table 2. Recommended Laboratory Tests to be obtained before Prescribing PrEP*.
  - Assessment for symptoms or signs of acute HIV infection, including a febrile, “flu”-, or “mono”-like illness in the previous 6 weeks. (A2)
  - Evaluation of concomitant medications to identify nephrotoxic drugs or drugs that have interactions with the PrEP regimen. (A3)
  - Inquiry about the individual’s reproductive plans. (A3)
- Clinicians should prescribe PrEP only after receiving a negative 4th generation (recommended) or 3rd generation (alternative) HIV test within 1 week of planned PrEP initiation. (A3)
- If the HIV test result is not available during the patient visit, the clinician should contact the patient to discuss the test result once it is available; if the result is negative, then the clinician should contact the patient’s pharmacy to prescribe PrEP. (A3)
- See NYSDOH AI guidelines *Diagnosis and Management of Acute HIV and HIV Testing*

### Prescribing PrEP

- Clinicians should initially prescribe only a 30-day supply of PrEP.
  - At the 30-day follow-up visit, once adherence and tolerance is assessed a 60-day supply can be prescribed.
  - At the 3-month follow-up visit, and at 3-month intervals thereafter, a 90-day supply can be prescribed if adherence and tolerance remain stable and patients remain HIV uninfected.
    - See the PrEP Management Checklist, p. 25 for a schedule of visits and follow-up assessments in the first year of a patient’s use of PrEP. (A3)

### Time to Protection

- Clinicians should educate patients about the time required to achieve protective concentrations of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for PrEP (A2):
  - 7 days of daily PrEP use for protection with receptive anal sex.
  - 20 days of daily PrEP use for protection with receptive vaginal sex, insertive anal or vaginal sex, and injection drug use.

### Follow-Up

- Upon initiation of PrEP, clinicians should instruct patients to notify their care provider immediately if they experience side effects. (B3)
- Within 2 weeks of PrEP initiation, clinicians should follow up with the patient to: (B3)
  - Ensure the prescription was filled.
  - Troubleshoot problems with payment and connect the patient to resources for payment if needed.
  - Inquire about side effects and proper use of PrEP.
- At each visit, clinicians should: (B3)
  - Assess adherence and discuss strategies for maintaining adherence.
  - Discuss risk reduction in the context of the individual’s sexual health and/or injection drug use needs.
  - Offer condoms, and, if appropriate, syringe access.
  - Manage side effects.

### Adherence and Retention in Care

- Clinicians should provide adherence counseling during every patient contact. (A3)

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**✓ ALL RECOMMENDATIONS – CONTINUED****Risk Reduction**

- As an approach to decreasing acquisition of HIV and other STIs, clinicians should offer male and female condoms to all patients, including those using PrEP, at each visit. (A3)
- For patients who inject drugs, and others who misuse mood-altering drugs, clinicians should:
  - Make referrals for substance use treatment and mental health support as appropriate (A3)
  - Prescribe clean syringes and needles or refer to needle-exchange programs as indicated. (A2)
    - See NYSDOH: Expanded Syringe Access Program and Syringe Exchange Programs
- For patients in serodiscordant relationships, clinicians should discuss at each visit the benefits and risks of treatment as prevention (TasP) alone versus TasP + PrEP strategies for preventing transmission of HIV. (B3)

**Monitoring**

- Clinicians should perform routine monitoring of patients using PrEP according to the recommendations in Table 3, *Recommended PrEP Monitoring and Laboratory Testing*, below.

**HIV Testing**

- Clinicians should obtain a 4th-generation (recommended) or 3rd-generation (alternative) laboratory-based HIV screening test before initiation of PrEP and every 3 months while a patient is using PrEP. (A3)
- Whenever patients present with symptoms or signs consistent with acute retroviral syndrome, clinicians should perform HIV testing immediately according to guidelines for the evaluation of acute HIV infection. (A2)
  - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV*
  - See *HIV Acquisition While Using PrEP* in this guideline, p. 36

**Renal Function**

- At the following intervals, clinicians should perform renal function testing, including creatinine, and calculated GFR: (B3)
  - Before initiating PrEP with TDF/FTC.
  - At 3 months after initiation.
  - At least every 6 months for the duration of PrEP.
- If the patient develops a calculated GFR  $\leq 50$  mL/min on PrEP with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), then PrEP should be discontinued. (A2)
- Clinicians should perform urinalysis at baseline and annually. (B3)

**HCV Screening**

- Clinicians should obtain annual HCV screening for patients using PrEP. (A3)

**STI Screening**

- Clinicians should assess patients for signs and symptoms of STIs, including syphilis and gonococcal and chlamydial infections, as part of a sexual history at every visit. (A3)
- Clinicians should perform ongoing screening for syphilis, gonococcal, and chlamydial infections as specified in Table 3: *Recommended PrEP Monitoring and Ongoing Laboratory Testing*, p. 31.

**Pregnancy Screening and Management**

- Clinicians should perform pregnancy testing in women of childbearing potential as follows (A3):
  - Every 3 months for women if effective contraception is not in use or whenever a new STI is diagnosed.
  - Annually when effective contraception is in use.
- Clinicians should counsel patients in serodiscordant relationships who are using PrEP and wish to conceive that the partner with HIV infection should achieve complete and sustained viral suppression for at least 6 months before attempts to conceive. (A2)

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**✓ ALL RECOMMENDATIONS – CONTINUED****Discontinuing PrEP**

- Clinicians should discontinue PrEP in any patient who:
  - Has a confirmed positive HIV test. (A1)
  - Develops a calculated GFR  $\leq 50$  mL/min on PrEP with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). (A2)
  - Does not adhere to HIV testing requirements. (A3)
- Clinicians should closely monitor patients who have chronic HBV infection for potential rebound when PrEP with TDF/FTC is discontinued and develop an alternative treatment plan. (A2)
- PrEP should also 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 of acquiring HIV.

**Suspected Acute HIV**

- Clinicians should inform patients with suspected acute HIV infection about the increased risk of transmitting HIV during acute HIV infection (A2)

**Asymptomatic Patients**

- For asymptomatic patients who receive a reactive HIV screening result while using PrEP, clinicians should:
  - Discontinue PrEP immediately; if supplemental laboratory testing does not confirm HIV infection, PrEP may be resumed. (A1)
  - In consultation with an experienced HIV care provider, recommend initiation of ART with at least 3 fully active antiretroviral medications. (A1)
  - Perform supplemental diagnostic testing according to the CDC HIV testing algorithm. (A1)
  - Ask about medication interruption of any duration and identify any access or adherence barriers. (A3)
- If supplemental laboratory testing confirms HIV infection, clinicians should:
  - Perform HIV RNA testing, if not already obtained as part of the diagnostic algorithm for suspected acute HIV infection, to measure viral load. (A2)
    - See NYSDOH AI guideline *Diagnosis and Management of Acute HIV Infection*
  - Perform HIV genotypic resistance testing. Adjustments to the initial ART regimen can be made once genotypic resistance results are available or when considering side effects. (A2)
    - See NYSDOH AI guideline *Selecting an Initial ART Regimen*

**Symptomatic Patients**

- For patients who present with any symptoms of acute retroviral illness and for whom acute HIV infection is suspected, clinicians should perform a plasma HIV RNA assay in conjunction with an HIV screening test. (A2)
- The patient should continue PrEP until results are available, preferably within 1 week. (B3)
  - See NYSDOH AI guideline *HIV Testing*
- For patients who receive a nonreactive screening result with HIV RNA  $\geq 5,000$  copies/mL:
  - A clinician can make a presumptive diagnosis of HIV infection. (A2)
  - Recommend ART and perform HIV genotypic resistance testing; adjustments to the initial ART regimen can be made according to genotypic resistance results or side effects. (A2)
    - See NYSDOH AI guideline *Selecting an Initial ART Regimen*
- For patients who receive a nonreactive HIV screening result but have detectable HIV RNA with  $< 5,000$  copies/mL, repeat HIV RNA to exclude a false-positive result after discontinuation of PrEP; ART may be offered as described above for patients with a nonreactive screening result with HIV RNA  $\geq 5,000$  copies/mL while awaiting results from repeat HIV RNA testing. (A2)

## How This Guideline Was Developed

Medical Care Criteria Committee, October 2017

The NYSDOH AI protects and promotes the health of New York State's diverse population through disease surveillance and the provision of quality services for prevention, health care, and psychosocial support for those affected by HIV/AIDS, STIs, viral hepatitis, and related health concerns. In addition, the NYSDOH AI promotes the health of LGBT populations, substance users, and the sexual health of all New Yorkers. In response to the availability of an effective PrEP regimen to prevent acquisition of HIV infection among people at risk, the AIDS Institute prioritized development of this clinical practice guideline, *Pre-Exposure Prophylaxis to Prevent HIV Acquisition*.

**Committee Makeup:** Members of the MCCC (see Box A1: *MCCC Leaders, Members, and PrEP Guideline Reviewers*, below) were appointed by the NYSDOH AI to ensure representation of clinical practice in all major regions of the state, relevant medical disciplines and sub-specialties, key NYS agencies, community stakeholders, and patient advocates. Individuals confirmed as Committee members are required to disclose any potential conflicts of interest; disclosures are reviewed and approved by the NYSDOH AIDS Institute Office of the Medical Director (see *Funding and Financial Disclosure of Potential Conflicts of Interest*, below).

**Committee Role:** Committee members actively participate in guideline development, including evidence review, drafting of recommendations and text, manuscript review, consensus approval of all recommendations, and rating of recommendations.

**Committee Leadership:** Working with the lead author, the MCCC Planning Group of Committee leaders reviewed and refined the manuscript, facilitated consensus approval of all recommendations, and addressed feedback from external peer and consumer reviewers.

**Johns Hopkins University (JHU) Editorial Role:** The JHU editorial team coordinated, guided, and documented all Committee activities, and edited the guideline material for clarity, flow, and style.

### **MCCC Planning Group (all Committee members and reviewers are listed in Box C1, below)**

- Samuel T. Merrick, MD, Chair
- Joseph P. McGowan, MD, FACP, FIDSA, Vice-Chair
- Judith A. Aberg, MD, FIDSA, FACP, Chair Emeritus
- Charles J. Gonzalez, MD, AIDS Institute Associate Medical Director for Science and Policy
- Christopher J. Hoffmann, MD, MPH, JHU Principal Investigator

### **AIDS Institute and JHU Editorial and Program Management Team**

- Laura Duggan Russell, MPH, AIDS Institute Guidelines Program Coordinator
- Mary Beth Hansen, MA, JHU Guidelines Project Director
- Christina Norwood, MS, ELS, JHU Senior Editor
- Johanna Gribble, MA, JHU Medical Editor
- Jen Ham, MPH, JHU Medical Editor
- Jesse Ciekot, JHU Program Coordinator

**Box A1: MCCC Leaders and Members (when this guideline was developed), and PrEP Guideline External Reviewers**
**Leadership**

- *Chair:* Samuel T. Merrick, MD, New York Presbyterian–Weill Cornell, New York, NY
- *Vice–Chair:* Joseph P. McGowan, MD, FACP, FIDSA, North Shore University Hospital, Manhasset, NY
- *Chair Emeritus:* Judith A. Aberg, MD, FIDSA, FACP, Icahn School of Medicine at Mount Sinai, New York, NY
- *Medical Director:* Bruce D. Agins, MD, MPH, New York State Department of Health (NYSDOH) AIDS Institute (AI), New York, NY
- *Deputy Medical Director:* Lyn Stevens, MS, NP, ACRN, New York State Department of Health (NYSDOH) AIDS Institute (AI), Albany, NY
- *JHU Principal Investigator:* Christopher J. Hoffmann, MD, MPH, Johns Hopkins University School of Medicine, Baltimore, MD

**Contributing Members and Liaisons**

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- Rona M. Vail, MD, Callen–Lorde Community Health Center, New York, NY
- William M. Valenti, MD, FIDSA, Trillium Health, Rochester, NY (Liaison for the Medical Society of the State of New York)

**External Peer Reviewers**

- Robert Murayama, MD, MPH, FACP, Chief Medical Officer, APICHA Community Health Center, New York, NY
- Peter Meacher, MD, AAHIVS, FAAFP, Chief Medical Officer, Callen–Lorde Community Health Center, New York, NY

## Funding and Disclosure of Potential Conflicts of Interest (COIs)

**Funding:** New York State funds supported development of the *PrEP to Prevent HIV Acquisition* guideline through a grant awarded to the Johns Hopkins University School of Medicine, Division of Infectious Diseases, from the New York State Department of Health AIDS Institute.

**Conflicts of interest:** All active MCCC members, invited consultants and coauthors, peer reviewers, and program staff are required to disclose financial relationships with commercial entities, including gifts that may be actual conflicts of interest or may be perceived as conflicts. These individuals must disclose financial relationships annually, for themselves, their partners/spouses, and their organization/institution. On their annual disclosures, MCCC members are asked to report for the previous 12 months and the upcoming 12 months. Box A2, below, lists reported conflicts.

**Management of COIs:** All reported financial relationships with commercial entities are reviewed by the NYSDOH AI guidelines program to assess the potential for undue influence on guideline recommendations made by the Committee. For the Committee members reporting conflicts, it was determined that because there is just one FDA-approved drug regimen for PrEP and a preponderance of evidence in support of that regimen for PrEP, the potential for exertion of undue influence on recommendations was exceedingly low to non-existent.

All guideline recommendations received consensus approval of the full MCCC, and the final review and approval of the recommendations was performed by the Committee Chair, and the NYSDOH AI Medical Director and Deputy Medical Director, none of whom reported conflicts of interest.

External peer reviewers were also required to submit conflict of interest/financial disclosure information, which were similarly screened. Neither peer reviewer reported conflicts.

<b>Box A2: Reported Conflicts of Interest/Financial Disclosure Results</b>	
<b>Committee Member's Guideline Role</b>	<b>Relationships disclosed for the previous and/or upcoming 12 months</b>
Planning Group Member	Research support: Gilead, ViiV; scientific advisor: Merck
Planning Group Member	Scientific advisor: Merck
Committee Member	Scientific advisor: GFORCE
Committee Member	Consultant: Roche Diagnostics
Committee Member	Consultant: Gilead, Merck, ViiV, BMS

## Evidence Collection and Review

The NYSDOH AI guideline development process is based on a strategic search and analysis of the published evidence. Box A3 illustrates the evidence review and selection process.

### Box A3: Evidence Collection and Review Processes

- NYSDOH AI and MCCC defined the goal of the guideline: To provide evidence-based clinical recommendations for primary care management of PrEP to prevent HIV acquisition.
- MCCC appointed a lead author, who conducted a systematic literature search in PubMed using MESH terms. All searches were limited to studies that 1) were published within the previous five years; 2) involved only human subjects; and 3) were published in English.
- Lead author reviewed studies identified through searches, and excluded based on the following criteria:
  - Based on publication type, study design, participants and clinical relevance to the guideline.
- Author and editorial staff conducted additional searches using PubMed and online databases to identify:
  - Studies published prior to the 5-year search limit
  - Studies published during the guideline development process
  - Recent conference abstracts
  - Older studies known to provide strong evidence in support of specific recommendations or to undergird expert opinion
  - New York State epidemiologic data
- Lead author developed and all MCCC members reviewed and approved evidence-based guideline recommendations:
  - Planning group reviewed, deliberated, refined, and approved draft recommendations.
  - MCCC members reviewed, provided written comment on, deliberated, and reached consensus on recommendations
  - Planning group reviewed the cited evidence and assigned a two-part rating to each recommendation to indicate the strength of the recommendation and the quality of the supporting evidence; consensus reached on ratings.
  - Additional evidence identified and cited during the rating process (see Box C4, below)
- Ongoing Update Process
  - JHU editorial staff will surveil published literature on an ongoing basis to identify new evidence that may prompt changes to existing recommendations or development of new recommendations
  - JHU editorial staff will ensure that the MCCC reviews new studies at least 4 times per year, and more often if newly published studies, new drug approval, or drug-related warning indicate the need for an immediate change to the published guideline.
  - JHU editorial staff will track, summarize, and publish ongoing changes to the guideline
  - MCCC reviews and approves substantive changes to, additions to, or deletions of recommendations
  - The Committee will initiate a full review of the guideline 4 years after the original publication date
  - NYSDOH AI will publish a comprehensive update 5 years after the original publication date

## Recommendation Development and Rating Process

The clinical recommendations presented in this guideline were developed by consensus based on a synthesis of the current evidence collected through the systematic search described above. If no data were available, the recommendations are based on expert opinion, and this status is indicated in the rating and in the text.

The Planning Group met via monthly teleconferences over approximately 12 months to finalize the guideline and reach consensus on recommendations and rationale. Once consensus among the Planning Group members was reached, the guideline was reviewed by the full MCCC, and consensus was reached on all recommendations. These deliberations were conducted by teleconference; MCCC members were invited to submit comments in writing as well. Committee review discussions were recorded, and recordings were reviewed carefully to ensure that all decisions and changes were captured and integrated into the manuscript.

Members of the Planning Group then individually reviewed the evidence for each recommendation and assigned a two-part rating (see Box A4). The individual ratings were compiled into a report distributed to all raters, and conference call discussions were held to deliberate ratings for which consensus was needed. Once all raters agreed on the interpretation of evidence and ratings for all recommendations, the guideline was sent to the NYSDOH AI for review and approval.

<b>Box A4: AIDS Institute HIV Clinical Guidelines Program Recommendations Rating Scheme</b>	
<b>Strength of Recommendation</b>	<b>Quality of Supporting Evidence</b>
A = Strong	1 = At least 1 randomized trial with clinical outcomes and/or validated laboratory endpoints
B = Moderate	2 = One or more well-designed, nonrandomized trial or observational cohort study with long-term clinical outcomes
C = Optional	3 = Expert opinion

## External Review

Two external peer reviewers recognized for their experience and [expertise in HIV primary care](#) were identified by program leaders (see Box A1). These individuals submitted a financial disclosure statement for the purpose of identifying potential conflicts of interest before participating as peer reviewers; neither disclosed financial relationships with commercial entities in the 12 months prior or the 12 months following submission of the disclosure.

Peer reviewers were asked to review the guideline for accuracy, balance, clarity, and practicality of the recommendations for primary care providers. The Planning Group addressed peer review feedback; any conflicting opinions were resolved by the Committee chairs. Members of NYSDOH AI Community Advisory Committee also reviewed and commented on the guideline.

## Guideline Updates

Members of the MCCC will monitor developments in PrEP use and management in an ongoing structured manner to maintain guideline currency. Once the guidelines are published on the program website: [www.hivguidelines.org](http://www.hivguidelines.org), any updates will be made to the HTML document as needed as new peer reviewed literature on PrEP is published and if new drug regimens are approved by the FDA.

Notification of newly published studies will be automated, and the Planning Group will review new data at least every 4 months. Newly published data that provide support for existing recommendations will be cited in the text, and the studies will be added to the reference list(s).

If newly published data prompt a revision to recommendations or rationale, the Planning Group will propose appropriate edits and determine whether the changes warrant review and approval by the entire MCCC. If MCCC review is required, a conference call will be convened for that purpose. Deletion of existing recommendations, addition of any new recommendations, and/or substantive changes to existing recommendations will prompt MCCC review and consensus.

If a new medication or formulation is approved, the Planning Group will be convened via conference call to examine the data, consider inclusion in the guideline, and determine the need for MCCC review and approval.

The full guideline will be reviewed and updated on the 4th anniversary of original publication to prepare for publication of an updated guideline on or before the 5th anniversary of original publication.

**About this guideline:** This guideline has been downloaded from the website of the New York State Department of Health AIDS Institute Clinical Guidelines Program: [www.hivguidelines.org](http://www.hivguidelines.org). The website is managed by the Clinical Guidelines Program in the JHU School of Medicine, Division of Infectious Diseases, on behalf of the NYSDOH AIDS Institute. Visit the website for information about the program, the guideline committees, and other related guidelines and materials.

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