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Oral Pre-Exposure Prophylaxis (PrEP) for HIV Prevention in Adolescents and Young Adults

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Abstract

Purpose of review—To review the literature about oral pre-exposure prophylaxis (PrEP) for HIV prevention, with specific focus on adolescents.

Recent findings—Use of PrEP reduces new HIV infections among men who have sex with men, heterosexuals, and people who inject drugs. One combination antiretroviral medication is approved for PrEP in the U.S. for adults. Limited data suggest that PrEP is safe for use in youth, although declines in adherence to PrEP over time suggest the need for adherence interventions specifically targeting youth. Safety concerns related to PrEP include potential negative impacts on bone density and renal function, as well as potential increases in riskier sexual behaviors. The U.S. Public Health Service has published guidelines for PrEP use in adults.

Summary—Current data suggest that PrEP use is safe in adolescents; however, further research is needed on the potential impact of long-term PrEP use on bone density and kidney function.

Keywords

HIV prevention; pre-exposure prophylaxis; adolescents; PrEP

Introduction

Daily oral pre-exposure prophylaxis (PrEP) - or the use of antiretroviral medications by adults who are uninfected with human immunodeficiency virus (HIV) - decreases rates of new HIV infections. Use of a tenofovir-based regimen reduced new HIV infections among men who have sex with men (MSM) and transgender women by 44%.[1] heterosexual men

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NOTE: The last name of the first author is "Mullins." "L. Kowalczyk" are middle names.

Conflict of Interest

Tanya L. Kowalczyk Mullins and Corinne E. Lehmann each declare no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

and women by 62%, [2] heterosexuals with HIV-infected partners by 67–75%, [3] and people who use injection drugs by 49%. [4] The U.S. Food and Drug Administration (FDA) approved the use of a combination pill with tenofovir disoproxil fumarate-emtricitabine (TDF/FTC; Truvada®) for PrEP among adults, [5] and the U.S. Public Health Service has published guidelines to aid clinicians who are prescribing PrEP. [6, 7]

Adherence to drug and time on drug are critical factors for optimizing effectiveness. Greater adherence to PrEP is linked to higher levels of protection. MSM and transgender women with detectable tenofovir levels had 92% reduction in HIV infections. [1] Patient reported use of PrEP in the past 30 days was associated with 78% reduced risk of HIV among heterosexual adults, [2] and plasma concentrations of tenofovir that were consistent with taking PrEP daily were associated with 88–91% reduction in new infections among heterosexual adults with HIV-infected partners. [8] However, perfect adherence to daily PrEP may not be necessary to achieve high levels of protection, at least for some anatomic areas of exposure. Among MSM taking combination tenofovir-emtricitabine, no new HIV infections were documented among those taking 4–6 doses or more per week, [9] suggesting that high levels of protection can be achieved in the rectal compartment with incomplete adherence. However, more perfect, daily adherence is required in order to achieve protection in the female genital tract. [10] Similarly, the time required to achieve maximum concentrations of tenofovir in different anatomic areas varies. Pharmacologic studies suggest that maximum tenofovir concentrations are reached with 7 days of daily dosing for rectal tissue and 20 days of daily dosing for blood and cervicovaginal tissue. [6, 11, 12]

Data about PrEP use among adolescents are limited. Two studies have been published from the U.S. Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN): one in 18–22 year-old MSM (ATN 110) [13] and one in 15–17 year-old MSM (ATN 113). [14] Both studies were open-label demonstration projects and thus not designed to assess efficacy. In the study of 18–22 year-olds, 200 participants enrolled, and 70% completed the study at week 48. Most (60%) found taking a daily pill to be acceptable. In the study of 15–17 year-olds, 72 participants started PrEP, and 46 of these completed the 48 week study. Adherence to PrEP – defined as drug levels consistent with taking 4 or more doses per week – in both of these studies was higher (approximately 49–57%) during the first 12 weeks when visits occurred monthly. Adherence declined when visits occurred every 3 months – which is the recommended interval for follow-up for PrEP according to the current U.S. guidelines. [6] By week 48, adherence to 4 or more doses per week had decreased to 34% among the 18–22 year-olds and 22% among the 15–17 year-olds. These data suggest that younger PrEP users may require more frequent follow-up and that interventions specifically designed to support adherence in youth may be beneficial. To date, no medication has been approved by the U.S. FDA for use as PrEP in patients under age 18.

Safety Issues and PrEP

Medication Side Effects

Antiretroviral medications can have side effects. Ten percent of users of Truvada® have mild to moderate symptoms of nausea, abdominal pain, and headache in the first month of use. [5] Providers prescribing to adolescents may need to provide “preemptive” anticipatory

guidance regarding these potential side effects.[15] The use of tenofovir can be associated with nephrotoxicity. The current U.S. PrEP guidelines allow for PrEP use in patients with an estimated creatinine clearance (eCrCl) ≥ 60 ml/min.[6] Among adults using PrEP, 15% had an estimated glomerular filtration rate (eGFR) <70 ml/min on follow-up testing, and 0.6% stopped PrEP due to low eGFR. In this study, younger age was associated with a reduced risk of decline in eGFR. Factors significantly associated with decreased eGFR during PrEP use included age >30 years and eGFR <90 ml/min at baseline; patients with diabetes had a borderline increased risk for decline in eGFR. These findings are consistent with data from the original U.S. PrEP Demonstration Project.[16] Among MSM ages 18–22 using PrEP in ATN 110, only one participant had a grade 1 elevation in creatinine that subsequently resolved.[13] Among MSM ages 15–17 taking PrEP in ATN 113, no renal events were reported. However, 13 of the 260 original participants who were eligible to participate ultimately were not enrolled in the study due to meeting renal exclusion criteria of eGFR <75 ml/min or other electrolyte or urine abnormalities.[14] As the incidence of discontinuation of PrEP due to renal toxicity was very low in those with eGFR ≥ 90 ml/min at baseline, Marcus et al. suggest that less frequent renal monitoring than is currently recommended may be appropriate in these patients.[16]

Tenofovir may also negatively impact bone density. Among adults taking PrEP, statistically significant decreases in bone mineral density (BMD) of 1.42% at the spine and 0.85% at the hip were seen at 24 weeks. The decrease in BMD was inversely related to serum tenofovir levels, suggesting a dose response relationship. However, there was no increase in overall incidence of low BMD or fractures.[17] Further study of this cohort showed that, on average, BMD returned to baseline levels one year after PrEP was stopped.[18] Among MSM PrEP users ages 18–22 years participating in ATN 110, modest but significant decreases in BMD from baseline to week 24 were seen in the hip and whole body. Between weeks 24 and 48, significant decreases in BMD were seen at the hip, but no further losses were observed at the spine or whole body. This cohort also had baseline median BMD Z-scores below zero, suggesting lower BMD than would be expected in healthy young men. [13] Among 43 15–17 year-old MSM in ATN 113, there was no change in BMD from baseline to week 48 at the hip and spine, but total body BMD Z-score decreased significantly. Subgroup analysis did not reveal a correlation between BMD and drug levels. No fractures occurred during the study.[14] An analysis of 101 participants from both ATN 110 and 113 showed that greater drug exposure was associated with greater decline in hip BMD at week 48. Higher drug exposure also was correlated with lower fibroblast growth factor 23 and higher parathyroid hormone levels, leading the authors to speculate that tenofovir use may lead to a “functional vitamin D deficiency.”[19] Larger sample sizes and longer term monitoring of BMD and bone turnover markers in adolescents using PrEP are needed to draw further conclusions about bone health safety in younger PrEP users who are at the peak of bone mass accrual.

Risk Compensation

The majority of adult MSM report that condoms and safer sex are important, even when using PrEP.[20] Among some patients however, PrEP use reduced perceived risk of acquiring HIV, leading to decreased use of condoms (termed “risk compensation”) and

possible increased acquisition of other sexually transmitted infections (STIs). Some patients using PrEP have reported increased number of condomless anal sex partners,[21] decreased condom use,[22] greater number of condomless sex partners,[22] or greater frequency of condomless oral sex than nonusers.[22] In other studies, users of PrEP reported a decrease in number of partners but no change in condomless sexual behavior,[23] and young 16–20 year old MSM reported significantly higher rates of condomless sex when they were using PrEP compared to when they were not using PrEP.[24] Two studies have shown high rates of STIs during PrEP use,[23, 16] suggesting that STI screening may need to occur more often than every 6 months as currently recommended by the U.S. PrEP guidelines.

Adherence and Retention

Retaining patients in care is critical for maximizing adherence to PrEP.[25] Concerns have been raised that inadequate adherence to PrEP may lead to acquisition of HIV infection and possibly resistant HIV virus. In one study of adults, no acute seroconversions were found in 850 person/years use of PrEP. Two individuals seroconverted after they started PrEP and subsequently lost health insurance coverage, which presumably led to discontinuation of PrEP.[16] In ATN 110, 4 seroconversions occurred: none of these participants had detectable levels of tenofovir, and no antiretroviral resistance was detected.[13] In ATN 113, 3 individuals seroconverted, none of whom had resistant virus. Drug levels correlated with taking less than a mean of 2 doses per week at the likely time of HIV acquisition.[14] While these results are reassuring, there have been case reports of HIV acquisition in people with known high levels of adherence.[26, 27] Clinicians need to recognize the symptoms of potential seroconversion in PrEP users and obtain regular HIV testing.

Retaining adolescents in care may be a critical component to PrEP success. In a study of adult MSM starting PrEP, only 47% of those who started PrEP were retained at 13 months, and those diagnosed with an STI were less likely to be retained in care.[28] In a follow-up survey of PrEP users from the original U.S. PrEP demonstration project, participants reported high interest in continuing PrEP, but only 38% continued it after the original 48 week study.[29] Respondent sociodemographic factors including older age, higher education, higher income, having health insurance, and having a regular primary care provider were significantly associated with continuing PrEP. Cost was the greatest perceived barrier to receiving PrEP, followed by lack of health insurance and access to care.[29] Strategies to retain younger patients in PrEP care may need to be comprehensive and multi-focal, and may need to include assistance in getting health insurance or medication coverage through patient assistance programs, access to care and transportation, and continued support of adherence. More frequent follow-up visits than is suggested by the guidelines may be necessary for adolescent PrEP users given the striking drops in adherence after follow-up visit frequency decreased to quarterly in the ATN 113 trial.[14]

Patient and Clinician Attitudes toward PrEP

Awareness of PrEP among Potential PrEP Users

Studies of adult MSM and transgender women report that 43–74% of participants are aware of PrEP,[30–32] with 7% of participants reporting current PrEP use[30] and 9% reporting

PrEP use in the past 3 months.[22] Interest in taking PrEP is fairly high, with 44–55% of MSM reporting willingness to take PrEP.[30, 31, 33] Willingness to take PrEP among adult MSM in California was associated with Hispanic/Latino ethnicity, greater concern about acquiring HIV, fewer concerns about side effects, less medical mistrust, fewer concerns about one's ability to adhere to PrEP, and greater perceived benefits of PrEP.[31] Also among adult MSM, current PrEP use was associated with greater income, having had receptive condomless anal sex in the prior 6 months, having sex with an HIV-infected partner, and being diagnosed with an STI in the past year -[34] suggesting that people using PrEP are indeed at high risk of HIV.

Awareness of PrEP is somewhat lower among other potential PrEP users.[35] Only 33% of female sex workers were aware of PrEP, although 65% were interested in taking it.[36] In another study, 60% of women would consider taking a daily pill in order to protect themselves from HIV.[37] Among adult transgender women, 31% were aware of PrEP, 5% had taken it, and 69% were interested in taking PrEP.[38] Awareness of PrEP among people who use drugs varies from 3% to 37%, [39–42] and interest in using PrEP varies from 33% to 67%. [39, 41] Because HIV-uninfected partners of HIV-infected people are an important target for PrEP, building awareness of PrEP among HIV-infected patients is critical: few HIV-infected adults (15%) were aware of PrEP, but following education, 89% of these adults reported being likely to recommend PrEP to a partner.[43] Less is known about awareness of PrEP among adolescents. Among black MSM ages 15–24 years, 39% were aware of PrEP, 8% were taking it, and 62% reported being willing to take PrEP.[44] Among adolescent and young adult transgender women, 64% reported awareness of PrEP.[45]

Attitudes toward PrEP among Potential and Actual PrEP Users

One obvious benefit of using PrEP was remaining HIV-uninfected and having additional protection against HIV.[45] PrEP was viewed as a critical advance in HIV prevention.[46] Using PrEP was associated with feeling responsible for one's health; others described PrEP as “liberating” and “empowering.”[47] Other benefits included improved intimacy between partners in serodiscordant relationships and improved feelings of hope.[45]

Numerous barriers to PrEP use have been reported, including concerns about cost of the medication and/or medical visits[22, 34, 48–50] and concerns related to insurance.[22, 51] Other barriers include lack of awareness about PrEP,[22] uncertainty about where to access PrEP,[22] concerns about sequelae associated with long term use,[34] concerns about side effects,[22, 48, 50] lack of access to clinicians to prescribe PrEP,[49, 52] concerns about disclosing risk behaviors,[52] inability to adhere to PrEP,[34] lack of interest in taking a daily medication,[48] and low perception of personal risk of HIV.[48, 50] Potential users voiced concerns about how to incorporate PrEP into their daily lives.[52] Adult women reported concerns about potential negative reactions to their taking PrEP by partners, family members, and friends. These women were also concerned that current PrEP guidelines may not consider them to be at sufficient risk of HIV to warrant PrEP.[51] Among a group of transgender men, additional concerns included financial concerns related to un/underemployment and the cost of time away from work in order to attend medical visits, as well as possible interactions between PrEP and testosterone or contraceptives.[49]

Stigma around PrEP use is a critical barrier to its success.[52] Such stigma includes the perception of others that someone using PrEP is HIV-infected.[46] PrEP was also perceived to be a prevention tool used by people who are sexually promiscuous[30, 46, 47, 53] or as “an excuse” for those not wanting to engage in other prevention behaviors.[53] Among a sample of MSM and transgender women, 70% believed that PrEP users would increase their risk behaviors, and 52% of participants in a community survey endorsed negative beliefs about people taking medication to prevent HIV.[54] Stigma associated with gay sexuality was also reported to be a barrier to PrEP use.[47] In order to avoid judgment by others, people may not disclose their use of PrEP, even though PrEP use was reported to *reduce* stigma that is associated with having HIV-infected sexual partners.[47]

PrEP and Clinicians Who Care for Adults

Most studies of clinicians and PrEP include primarily clinicians who care for adults. HIV specialists report high rates of PrEP awareness (92–98%),[55, 56] but lower rates of having prescribed PrEP (17–64%).[55, 57, 56] Rates of PrEP awareness were somewhat lower among generalist primary care providers (66–93%)[58, 56, 59, 60] as were rates of prescribing (7–17%).[56, 60] Generalists who were “PrEP adopters” (e.g., prescribing PrEP or referring patients to providers who prescribe PrEP) had higher self-rated knowledge about PrEP, perceived PrEP to be safe, and had fewer concerns about risk compensation.[58] Both HIV/infectious disease specialists and generalists reported greater willingness to recommend or prescribe PrEP to HIV-uninfected partners in serodiscordant relationships[61, 62] and lower willingness to recommend or prescribe PrEP to heterosexuals or people who inject drugs.[61, 62]

Barriers to providing PrEP included concerns about cost and insurance,[61, 63, 64, 56, 65–67] development of HIV viral resistance,[55, 63, 68, 64, 69, 65–67] and side effects/toxicity.[55, 63, 68, 64, 69, 65–67] Risk compensation was also a concern[63, 68, 64, 69, 66, 67] as was concern about patient adherence to PrEP and follow-up appointments.[61, 63, 68, 64, 66] Clinicians cited lack of knowledge about PrEP[56, 65] and need for further information about the effectiveness of PrEP[68, 65, 67] as other barriers. Less frequently reported barriers included lack of clarity about identifying candidates for PrEP,[64, 65] lack of interest among patients,[65] concerns about diversion of funding from other prevention strategies and/or HIV treatment,[64, 67] logistical barriers,[68, 64, 56] and clinician preference for patients to engage in behavior change instead of using PrEP.[69, 56] Clinicians voiced differing opinions about which healthcare providers would be best suited to provide PrEP, including HIV care providers, primary care providers, health departments, and/or STI clinics.[63, 69]

PrEP and Clinicians Who Care for Adolescents

Among clinicians caring for both HIV-infected and uninfected adolescents, 39% had prescribed PrEP to an adolescent under age 18 years, while 63% had prescribed PrEP to an adult.[70] Clinicians caring for adolescents identified many of the same barriers to prescribing PrEP that were reported by clinicians caring for adults, including concerns about: adherence, lack of patient willingness to take PrEP, patients having inaccurate perceptions of their risk of HIV, adherence to PrEP and monitoring visits, risk compensation,

logistical barriers, side effects/toxicity, effectiveness of PrEP in a clinical setting, and cost/insurance barriers.[71] However, barriers particularly relevant to prescribing to adolescents were also identified, including concerns about: parents (i.e., patients not being willing to use PrEP due to fear about parents finding out), confidentiality (i.e., disclosure of PrEP use on insurance explanation of benefits statements), potential inability of youth to understand risks/benefits of PrEP, and patients selling or sharing PrEP. Clinicians voiced concerns about prescribing PrEP to minor-aged patients due to the lack of FDA approval in this age group. [71] With respect to the CDC interim PrEP guidance, clinicians caring for youth noted that the guidance was in general compatible with their practices, but that some recommendations contained within the guidance – such as frequency of follow-up visits – would need to be tailored to meet the needs of adolescents.[72]

Experiences Implementing PrEP

Although an estimated 1.2 million U.S. adults meet indications for PrEP,[73] implementation studies demonstrate variable rates of uptake. Although some programs report high levels of PrEP uptake (49–59%),[74] others report lower rates of PrEP prescription (11–36%) and initiation (9–20%).[50, 32] Clinicians prescribing PrEP report challenges associated with providing PrEP that include: time required to help patients obtain coverage for the medication; need for flexibility in order to meet the needs of patients; supporting patient adherence to PrEP; and addressing risk compensation among some patients. However, these clinicians reported that few patients discontinued PrEP due to side effects.[75]

Current US Guidelines for PrEP

Consent and Legal Issues in Adolescents

To date, only the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg-emtricitabine 200 mg is approved in the U.S. for PrEP in “adults,” although a specific age range was not defined.[5] As the data to date for adolescents are sparse, the current guidelines state that “the risks and benefits of PrEP for adolescents should be weighed carefully in the context of local laws and regulations about autonomy in health care decision-making by minors.”[6] A 2012 review of U.S. state laws demonstrated that no state had expressly prohibited a minor’s access to PrEP or other HIV prevention methods.[76] As of 2018, 32 states explicitly include testing for and treatment of HIV among the STI services to which minors can consent.[77] However, inclusion of PrEP as a service to which minors can consent is not always stated explicitly in state laws. In 2017, the state of New York amended its laws to include HIV as one of the STIs for which minors can consent to treatment, and PrEP was expressly included as a service to which minors may consent without parental involvement. California state law also allows minors to consent to medical care for HIV prevention.[78] As laws regarding HIV prevention are rapidly changing, providers should consult local resources frequently. One resource is www.pleaseprepme.org, [79] which includes links to state resources and information for patients about PrEP. Additional resources can be found at the national AIDS Education and Training Center site at <https://aidsetc.org>. [80] Finally, providers need to consider confidentiality in the context of

medical billing: if adolescents use medical insurance provided by a parent(s), confidentiality may be inadvertently broken if the parent(s) receive an explanation of benefits statement from the insurer.[81]

Clinical Counselling and Testing for Providing PrEP (Table 1)

According to the U.S. PrEP guidelines, PrEP can be considered for patients without acute or established HIV infection. For MSM patients, factors that should lead clinicians to recommend PrEP include having any male sex partner in the past 6 months, not being in a monogamous relationship with an HIV-uninfected partner, and 1) any condomless anal sex in the past 6 months OR 2) any STI in the past 6 months. For heterosexual men and women, PrEP should be recommended to those who have been sexually active in the last 6 months, are not in a monogamous relationship with an HIV-uninfected partner, and 1) are a man who has sex with both men and women OR 2) use condoms inconsistently with partners of unknown HIV status who are at high risk of infection. For people who use injection drugs, clinicians should consider recommending PrEP if the person has used any non-prescription injection drugs in the past 6 months and 1) has shared injection equipment in the past 6 months OR 2) has been prescribed substance abuse treatment medication in the past 6 months OR 3) meets criteria for risk of sexual acquisition. Patients with known HIV-infected partners should be offered PrEP as well.[6]

Baseline testing includes HIV testing, renal panel, and hepatitis B and C serologies.[6] Although hepatitis B infection is treated with tenofovir, hepatic injury has occurred in HIV-infected patients in whom tenofovir is suddenly stopped. Therefore, patients who have hepatitis B infection need to be further assessed and informed of the risks of stopping tenofovir. The guidelines recommend that HIV testing occur every 3 months, as well as pregnancy testing in appropriate females. Providers are advised to give no more than a 90 day supply of PrEP in order to ensure HIV testing is occurring regularly and to provide other risk reduction and health care interventions, such as contraception. A renal panel and screening for other STIs should be completed at least every 6 months. The guidelines do not recommend a frequency for repeat hepatitis B and C testing.[6]

The guidelines recommend discussing the continued need for PrEP with patients at least every 12 months.[6] Situations that could prompt discontinuation of PrEP include lifestyle changes resulting in lower risk of HIV acquisition, struggles with adherence, and development of toxicity. If a patient becomes HIV-infected, providers should confirm HIV status and then urgently refer the patient to an experienced HIV care physician. The local health department also should be notified. Assessments of bone mineral density are not recommended. Therapeutic drug monitoring is left to the discretion of the prescribing provider. However, only a limited number of laboratories may provide this service, and drug levels only reflect recent dosing and not long-term adherence.[6]

Special Populations

Pregnant and breastfeeding women can take PrEP, although the guidelines acknowledge the limited data regarding safety in these situations.[6] However, the components of PrEP have been widely prescribed for HIV-infected women who are pregnant, and no adverse effects to

the woman or fetus have been found to date. Providers can report antiretroviral medication exposure in pregnancy to the Antiretroviral Pregnancy Registry at www.apregistry.com. The World Health Organization (WHO) recommends tenofovir-emtricitabine for pregnant and breastfeeding women for the prevention of HIV infection. In the 2015 WHO guidelines for PrEP,[82] the authors acknowledge that although fewer PrEP studies have been conducted in women, there have been no reported interactions between PrEP and hormonal contraception. [82] In studies of transgender women taking both estrogen-containing hormones and antiretrovirals for HIV treatment, neither tenofovir nor emtricitabine caused drug-drug interactions; however, the authors also noted the need for more study in this area.[83]

Conclusions

While uptake of PrEP among U.S. adults at high-risk for HIV acquisition has been slow, PrEP is a key breakthrough in the past decade that can help to slow the HIV epidemic in the U.S. While awareness of PrEP among some clinicians is high and has been increasing, prescribing rates have been slower to increase. Data on use of PrEP in adolescents are limited, and access to the medication by adolescents may be restricted by state laws and medical insurance practicalities. While the current evidence suggests that PrEP is safe for adolescents and young adults, further study is needed to examine the long-term safety of PrEP in relation to renal and bone health in growing adolescents. Providers, researchers, and advocates will need to continue to work on expanding access to PrEP for adolescents through advocacy in the health care, research, and legislative arenas.

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Table 1Summary of Current U.S. PrEP Guidelines (2014)⁶

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada®), 90 day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 6 months, test for bacterial STIs		
	Do oral/rectal STI testing	Assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

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Preexposure Prophylaxis for the Prevention of HIV Infection in the United States 2014 Clinical Practice Guideline.