HIV Preexposure Prophylaxis
A Review

James Riddell IV, MD; K. Rivet Amico, PhD; Kenneth H. Mayer, MD

IMPORTANCE About 40 000 Americans and 2 million people worldwide are newly infected with HIV each year. The combination antiretroviral regimen, tenofovir disoproxil fumarate (TDF)/emtricitabine, taken as a single pill once daily, has been shown to prevent HIV transmission but is used by fewer than 20% of people who could benefit in the United States.

OBSERVATIONS PubMed was searched on February 15, 2018, using the search terms pre-exposure, prophylaxis, HIV, and PrEP to identify English-language articles published between 2010 and 2018. Four placebo-controlled randomized clinical trials have demonstrated that preexposure prophylaxis (PrEP) with daily dosing of TDF/emtricitabine significantly reduces HIV acquisition in men who have sex with men, high-risk heterosexuals, and injection drug users who share injection equipment. The efficacy of daily TDF/emtricitabine exceeds 90% but is highly correlated with degree of adherence. TDF/emtricitabine is safe and well-tolerated. Only 2% of people discontinue PrEP because of adverse effects. Sexually transmitted infections are common among those using PrEP. Resistance to TDF/emtricitabine when used for PrEP is rare (<0.1%) and usually occurs when PrEP is inadvertently prescribed to individuals with undiagnosed acute HIV infection who have false-negative findings on HIV antibody/antigen testing due to HIV infection acquired within 7 to 10 days of testing. Effective methods are needed to identify individuals at high risk for acquiring HIV, ensure their access to PrEP, and maximize medication adherence.

CONCLUSIONS AND RELEVANCE TDF/emtricitabine is an effective and safe therapy for preventing HIV transmission. Increasing prescription of TDF/emtricitabine for patients at risk of acquiring HIV has the potential to reduce new HIV infections.


Despite significant advances in HIV treatment, HIV transmission remains common, with 39 782 new HIV diagnoses in the United States in 2016 and almost 2 million worldwide. Approximately 1 in 8 of the 1.2 million people living with HIV in the United States are unaware of their HIV status, and only half of those known to be infected are receiving effective antiretroviral therapy. Therefore, a large population of individuals is capable of transmitting HIV to others through sex without condoms or sharing of drug injection equipment. The risk of transmission per 10 000 exposures is approximately 138 for receptive anal intercourse, 8 for receptive penile-vaginal intercourse, and 63 for needle sharing.

Public health strategies to prevent HIV infection have included educational campaigns promoting safer sexual practices, expanded HIV testing, male circumcision, and prescribing antiretroviral drugs to HIV-infected individuals to decrease serum viral load, which decreases the risk of transmission. Between 2005 and 2014, a 19% decline in the number of new HIV infections (from 46 400 to 37 600) was observed in the United States, owing in part to these efforts; however, decreases in HIV transmission have not been uniform for all populations. For example, during this same period, the number of African American men aged 13 to 24 years diagnosed with HIV in the United States increased by 87% (from 2094 to 3923). Therefore, additional effective prevention strategies, such as higher rates of preexposure prophylaxis (PrEP) prescription in clinical practice, are needed.

The rationale for using antiretrovirals for PrEP to prevent transmission of HIV infection was initially based on animal studies and on case-control studies of humans using postexposure prophylaxis. For example, 1 study demonstrated that tenofovir disoproxil fumarate (TDF)/emtricitabine could prevent rectal mucosal transmission of simian/human immunodeficiency virus in macaques. In another study, health care workers who took zidovudine for postexposure prophylaxis after needle-stick injuries from HIV-infected patients were 80% less likely to contract HIV infection compared with those who did not use postexposure prophylaxis. In 2012, PrEP consisting of the fixed-dose, single-tablet combination TDF (300 mg) and emtricitabine (200 mg) was approved by the US Food and Drug Administration (FDA) for use in patients at high risk of HIV acquisition, including men who have sex with men (MSM), heterosexuals,
Since 2012, when TDF/emtricitabine was approved for PrEP, additional clinical studies have been performed demonstrating PrEP safety and effectiveness. However, clinicians prescribe PrEP for only a minority of at-risk individuals. This review summarizes evidence regarding HIV chemoprophylaxis, focusing on efficacy, risks, and benefits of HIV PrEP and on newer, ongoing HIV prevention strategies.

**Methods**

A literature search was performed in PubMed using the search terms pre-exposure, prophylaxis, HIV, and PrEP to identify English-language articles with dates of publication between 2010 and 2018 (n = 1030 studies on February 15, 2018). Specific articles for inclusion were selected by the authors based on clinical relevance and importance to prescribing practice.

**Efficacy of HIV Preexposure Prophylaxis**

Of the 2 studies that formed the basis for the FDA approval of PrEP, the iPrEx (Iniciativa Profilaxis Pre-Exposición [Preexposure Prophylaxis Initiative]) study enrolled 2499 HIV-uninfected MSM and transgender women in North and South America, South Africa, and Thailand who were randomly assigned to receive TDF/emtricitabine or placebo and followed up for a median of 1.2 years. HIV incidence was 3.7% among those randomized to receive placebo vs 2.1% among those randomized to receive TDF/emtricitabine (a 44% reduction) in the intent-to-treat analysis. The Partners PrEP study randomized 4747 heterosexual HIV-discordant couples in Kenya and Uganda to receive daily TDF/emtricitabine, TDF alone, or placebo. This trial was conducted prior to universal treatment for people living with HIV. Incidence of HIV was 1.5% for men and 2.8% for women randomized to receive placebo, and the intent-to-treat analysis found a decrease of 67% (17 transmissions among 1584 participants) among those randomized to receive TDF/emtricitabine compared with 52 HIV infections acquired among 1584 participants in the control group. Since the FDA approval of TDF/emtricitabine for use as daily oral PrEP, subsequent data from 4 trials of other at-risk populations confirmed these findings, including trials conducted in young African heterosexual and injection-drug-using populations, all of whom were followed up for at least 1 year.

HIV incidence in a study of 1219 heterosexual men and women in Botswana was 1.2% for those randomized to receive TDF/emtricitabine and 3.1% for those who received placebo, consistent with a transmission reduction rate of 62.2%. A study performed in Bangkok, Thailand, randomized 2413 injection drug users and found an HIV incidence of 0.5% per year among those who received daily TDF and 0.9% among those who received placebo (a 48.9% reduction). The efficacy of TDF/emtricitabine in preventing HIV transmission ranged from 44% to 75% in the 4 initial studies that demonstrated protection (Table 1). PrEP efficacy was directly correlated with medication adherence. Drug levels within the range shown to protect against HIV transmission were obtained in 50% to 81% of participants (Table 1). Post hoc analyses from these initial studies found that protection against HIV ranged from 92% to 100% among participants whose drug levels suggested that they

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**Box. Groups at Risk for Acquiring HIV Infection**

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<thead>
<tr>
<th>Adult Men Who Have Sex With Men</th>
<th>Sexual partner with HIV</th>
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<tr>
<td></td>
<td>Bacterial sexually transmitted infection (STI) in past 6 months</td>
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<tr>
<td></td>
<td>Receptive or insertive anal sex (past 6 months) AND history of inconsistent or no condom use (past 6 months)</td>
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<td>Commercial sex work (past 6 months)</td>
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<tr>
<th>Adult Heterosexual Men and Women</th>
<th>Sexual partner with known HIV infection</th>
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<tr>
<td></td>
<td>Women who wish to conceive who have a partner with HIV infection</td>
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<td></td>
<td>Bacterial STI (last 6 months)</td>
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<td></td>
<td>Sexual activity with partners of unknown HIV status (past 6 months) OR partners are at high risk of HIV infection (injection drug users or bisexual male partner) AND history of inconsistent or no condom use (past 6 months)</td>
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<td>Commercial sex work (past 6 months or ongoing) OR live in high-prevalence area or sexual network (HIV prevalence &gt;1.0%) and inconsistently use condoms</td>
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<table>
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<tr>
<th>Adult Injection Drug Users</th>
<th>HIV-positive injecting partner</th>
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<tr>
<td></td>
<td>Share injection equipment with others (past 6 months)</td>
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* These factors should lead to a discussion about preexposure prophylaxis (PrEP). Decisions about PrEP initiation should be individualized.
were taking the medication on a daily basis (intracellular tenofovir diphosphate levels of at least 700 fmol/mL in dried blood spot specimens). A study analyzing 972 individuals initiating open-label PrEP through Kaiser Permanente demonstrated 100% efficacy, with no seroconversions in patients who had at least 92% overall adherence.

Two studies did not demonstrate PrEP efficacy. The VOICE (Vaginal and Oral Interventions to Control the Epidemic) study randomized 3019 African women to receive daily oral TDF/emtricitabine, TDF alone, or placebo; the HIV incidence per year was 6.0%, 4.3%, and 4.2%, respectively. The FEM-PrEP (Preexposure Prophylaxis to Prevent the Acquisition of HIV-1 Infection) study, an open-label efficacy trial, randomized 544 MSM and 4747 heterosexuals to daily oral TDF or placebo, used “on demand” (4 pericoital tablets used over 3 d) or placebo, used “on demand” (4 pericoital tablets used over 3 d). Of data from the iPrEx study demonstrated that participants who had drug concentrations consistent with taking the medication at least 4 times a week did not develop HIV infection. Risk of HIV infection was decreased by more than 90% among women whose adherence was particularly important for women, because tenofovir has a shorter half-life in cervicovaginal tissues compared with colorectal mucosa. In rectal tissue, tenofovir and tenofovir diphosphate (the active intracellular moiety) concentrations are detectable for 14 days and are 100-fold higher than the concentrations in vaginal and cervical tissues. In cervicovaginal fluid, the half-life of tenofovir is 71 hours (50% longer than in plasma) and the half-life of emtricitabine is 40 hours (similar to plasma). Protective intracellular levels in vaginal tissue may not occur until day 21 of therapy, compared with day 7 in colorectal tissue for men. Post hoc analyses of data from the iPrEx study demonstrated that participants who had drug concentrations consistent with taking the medication at least 4 times a week did not develop HIV infection. Risk of HIV infection was decreased by more than 90% among women whose drug levels suggested daily use of TDF/emtricitabine, suggesting that PrEP is effective in women when daily adherence occurs.

Two additional randomized studies that focused on PrEP efficacy among MSM were completed in 2015 and 2016. The PROUD (Pre-exposure Prophylaxis to Prevent the Acquisition of HIV-1 Infection) study, an open-label efficacy trial, randomized 544 MSM accessing services at British public sexual health clinics to receive PrEP at study enrollment (n = 275) or to a “wait list” control group (n = 269) that received other HIV prevention services, including counseling, condoms, postexposure prophylaxis, and STI diagnosis and treatment but did not receive PrEP until after efficacy was demonstrated in the immediate treatment group. Intent-to-treat
analysis found that MSM assigned to immediate PrEP had an 86% decrease in HIV infections (1.3% per year incidence), compared with MSM in the delayed PrEP control group (9.0% per year), representing 3 HIV infections in the immediate PrEP group vs 20 in the control group.

The IPERGAY (Intervention Préventive de l’Exposition aux Risques avec et pour les Gays) study randomized French and Canadian MSM to receive pericortal TDF/emtricitabine (n=199) or matched placebo (n=201) for PrEP, with participants in the TDF/emtricitabine group instructed to take 2 pills between 2 and 24 hours before anal intercourse and 1 pill daily for the 2 days following sex but not to take more than 7 pills in a week. The intent-to-treat efficacy (ie, relative reduction in HIV incidence among those assigned to receive active medication compared with placebo) of this “on-demand” regimen was 86% in the original trial (2 HIV infections occurred in the treatment group and 14 in the placebo group). After participants in the placebo group were offered open-label TDF/emtricitabine, the efficacy increased to 97%. It is not clear how generalizable these findings are to other populations, since participants in this study averaged at least 1 episode of sex without condoms per week and were highly adherent to the study regimen. To date, only the government of France has approved this “non-daily” PrEP regimen as an acceptable alternative to daily use, although several other countries are evaluating this approach in demonstration projects. At present, daily dosing of TDF/emtricitabine is the only method recommended by the FDA until more data become available regarding this approach.

PrEP Open-Label and Demonstration Projects
After FDA approval of TDF/emtricitabine for PrEP in 2012, several demonstration projects (observational studies without a control group that seek to better understand PrEP delivery in a community or practice setting) sought to investigate how to deliver PrEP to high-risk, underserved communities and evaluate medication adherence. The DEMO project, which enrolled 557 MSM and transgender women in 2 STI clinics and a community health center, found that after 1 year, about 80% of PrEP users in San Francisco had protective drug levels (defined as levels consistent with more than 4 doses taken per week), although adherence appeared to be lower among African American participants (56.8%). An analysis of 32 months of clinical data from the Kaiser Permanente Health Maintenance Organization in the San Francisco Bay Area reported no new HIV infections among 667 PrEP users who had high STI rates (30% after 6 months), suggesting excellent adherence to TDF/emtricitabine in this particular group. In contrast, 2 parallel-group, open-label PrEP studies coupled with behavioral interventions in young MSM in the United States found annual HIV incidence rates of approximately 3% in 18- to 22-year-olds and almost 6% in youth aged 15 to 17 years. Drug levels were suboptimal, indicating poor adherence in 56% of the participants after 3 months. Only 34% had optimal adherence at the end of the 48-week study.

To address prevention of heterosexual transmission of HIV, the Partners PrEP Demonstration Project enrolled 1013 HIV-discordant couples in Kenya and Uganda and offered PrEP to the HIV-uninfected partner and antiretroviral treatment to the HIV-infected partner. Participants in this open-label, nonrandomized study had a 96% reduction in HIV transmission rates compared with historical controls. TDF used for PrEP in 1204 injection drug users in Bangkok conferred a 49% reduction in acquisition of HIV compared with 1207 participants receiving placebo. These additional data suggest that TDF/emtricitabine for use as PrEP in MSM, heterosexual couples, and injection drug users can be effective at preventing HIV infection if adherence is high.

PrEP Implementation
The Centers for Disease Control and Prevention estimates that 1.2 million adults in the United States aged 18 to 59 years may benefit from PrEP, including approximately 400 000 sexually active MSM, 600 000 sexually active heterosexuals, and 200 000 injection drug users. The identification of appropriate candidates for PrEP requires a thorough, periodic review of patients’ sexual and drug use patterns to identify patients at highest risk who would benefit from PrEP. Although overall PrEP prescribing is increasing in the United States, prescription of TDF/emtricitabine for PrEP is still less than optimal. Primary care physicians are well positioned to identify high-risk patients and prescribe PrEP.

Much of the reluctance among clinicians to prescribe TDF/emtricitabine is related to practical barriers. For example, clinicians may not be familiar with the International Classification of Diseases and Related Health Problems, Tenth Revision codes that may be used for such encounters (Table 2). The cost of the medication, required follow-up visits, and monitoring may present barriers for clinicians and patients. However, most private health care insurers cover PrEP and related monitoring costs, which consist of clinic visits once every 3 months with laboratory testing that includes HIV testing, screening for bacterial STIs, and assessment of renal function (Table 2). Medicaid also covers prescription costs, appointments, and laboratory tests. To cover the cost of the medication for uninsured or underinsured patients, there are programs available to obtain TDF/emtricitabine at low or no cost, including coupon cards, or the Gilead Sciences Inc medication assistance program, which covers prescription costs for those without insurance who meet certain income requirements.

Since adherence predicts efficacy, it is essential to ask about adherence and discuss its importance at each clinical visit. Adherence is usually assessed at the time of each quarterly interview by simply asking patients how many doses they have missed each week or month. As PrEP is prescribed by a more diverse group of clinicians such as primary care physicians, specialists, and clinicians providing care at STI clinics and community health centers, more at-risk patients can benefit.

Adverse Effects
Use of TDF in HIV-infected patients is associated with nephrotoxicity, with an incidence of 1.09/1000 person-years. Nephrotoxicity tends to develop late in the course of therapy (ie, approximately 55 ±28 months after start of therapy [range, 12-98]). Damage to the kidneys occurs as a result of interference with mitochondrial DNA synthesis when TDF is concentrated in proximal renal tubular cells over time. This leads to metabolic perturbations and loss of cellular function, which causes Fanconi syndrome or type IV renal tubular acidosis.

In the iPrEx study, 2% of patients receiving TDF/emtricitabine developed elevated creatinine levels, which normalized when medication was stopped, vs 1% of patients taking placebo (P = .08). In the IPERGAY trial, a decrease in glomerular filtration rate
rate to less than 60 mL/min was observed in 1% of those in the treatment group, which was not statistically significantly different than in the placebo group. In a subanalysis of the Partners PrEP study, which compared 776 patients receiving TDF/emtricitabine and 773 receiving placebo, there was no difference in the frequency of proximal renal tubule dysfunction (evaluated via a combination of serum and urine markers) over 24 months when the 2 groups were compared (1.7% vs 1.3%, respectively; \( P = .68 \)). Because of the small risk of nephrotoxicity, patients receiving TDF/emtricitabine for PrEP require monitoring of renal function once every 3 months.

TDF is also known to cause osteopenia, which is generally considered not clinically significant in most cases. Alterations in osteoblast gene expression caused by TDF have been shown to cause several deleterious effects on cellular function that lead to osteopenia. In a study performed in Botswana with 220 participants, half of whom took TDF/emtricitabine for PrEP, bone mineral density loss of more than 3% was greater in the treatment group than the placebo group (50% vs 32%, \( P = .04 \)). However, there was no difference in fracture rates: 7 in the treatment group vs 6 in the placebo group. No patients developed osteoporosis. In the iPrEx study, bone fracture rates were the same in each group (16 in the treatment group and 12 in the placebo group, \( P = .41 \)). Similarly, in the iPERGAY trial, there was no difference in bone fracture rates (2% vs 3%, \( P = .59 \)). Therefore, routine radiographic monitoring of bone mineral density is not indicated for patients initiating PrEP who do not have other risk factors for fracture, such as osteoporosis or osteopenia. With regard to other adverse effects associated with TDF/emtricitabine in the setting of PrEP, nausea (2% vs <1%, \( P = .04 \)) and weight loss (2% vs 1%, \( P = .04 \)) were the only symptoms observed significantly more frequently in the treatment group of the iPrEx study.

Adverse events related to PrEP use in pregnant women have been evaluated in 2 large efficacy studies. In the FEM-PrEP study, 2120 women in 3 sub-Saharan African countries received either TDF/emtricitabine or placebo to evaluate the efficacy of PrEP. In that study there were more pregnancy-related adverse events in the TDF/emtricitabine group (28 events, 11.2% incidence), compared with the placebo group (12 events, 7.5% incidence; \( P = .04 \)); however, there also were more pregnancies in the TDF/emtricitabine group (74) vs the placebo group (51). Specific information regarding which types of pregnancy-related adverse events occurred was not provided. There were no significant differences in spontaneous abortion or teratogenic effects between the groups in a preliminary analysis. An important caveat to this study is that adherence to study drug was only approximately 37%. In the Partners PrEP study, 4747 heterosexual HIV-discordant couples were randomized to receive TDF/emtricitabine or placebo to evaluate efficacy. In a post hoc analysis of this trial, PrEP had no effect on hormonal contraceptive effectiveness. Overall, the use of PrEP in pregnancy has not been systematically studied. However, because TDF/emtricitabine is classified as pregnancy category B, if a mother...
is at high risk, the benefits of preventing HIV infection would appear to outweigh the risks in this situation.44,45

Sexually Transmitted Infections
Patients who request PrEP are at risk for acquiring not only HIV infection but also other STIs. In the iPrEx study, 13% of volunteers were seropositive for syphilis at the time of initial screening, and more than one-third of patients were seropositive for herpes simplex virus 2.11 Similarly, in the IPERGAY study, 27% of patients had an STI, including syphilis, gonorrhea (oral, rectal, or urethral), or chlamydia at the beginning of the study.18 In the PROUD study, more than 60% of volunteers were diagnosed with an STI within the 12 months before enrollment.13 In a study evaluating 19,232 men (42.6% MSM) seeking care at a men’s health clinic between 2005 and 2015, bacterial STIs increased more than 8-fold, from 157 to 1319 diagnoses.46 Using PrEP was independently associated with a new STI on multivariable analysis, with a diagnosis rate of 24.55 per 100 person-years, compared with 10.39 per 100 person-years among non-PrEP users. The high prevalence of STIs before and after the initiation of PrEP illustrates the importance of routine STI screening among patients seeking PrEP. Therefore, every 3 months, screening urine samples and oral and rectal swabs (and optional cervical or vaginal swab) should be tested for gonorrhea and chlamydia using polymerase chain reaction and for syphilis using serology (rapid plasma reagin or VDRL test) (Table 2).26

Risk of Resistance
The use of TDF/emtricitabine as chemoprophylaxis for PrEP initially raised concerns that it could lead to the development or acquisition of resistant HIV.47 However, in efficacy studies performed to date, transmission of drug-resistance mutations have not been detected in patients who are adherent. In all of the major efficacy trials, only patients who had acute HIV infection with negative findings on screening HIV antibody tests (ie, were viremic but preseroconversion) developed resistant virus. Resistance develops in this setting because a dual-nucleoside combination (TDF/emtricitabine) used without a third antiretroviral drug rapidly selects for HIV resistance mutations. In both the iPrEx study and the PROUD study, 2 participants in each study assigned to the TDF/emtricitabine group who were subsequently found to be HIV-infected at the time of enrollment (likely with undiagnosed acute HIV infection) developed emtricitabine resistance.70,71 Resistance to TDF has been found in only 1 patient with unrecognized HIV infection in the TDF2 study, which examined the use of TDF/emtricitabine to prevent heterosexual transmission in Botswana.16 Two patients have been reported to have become infected with transmitted drug-resistant virus despite having therapeutic levels of tenofovir and emtricitabine.48,49 A third patient has been described who became infected with a susceptible strain despite drug levels consistent with appropriate dosing.50 Because of the risk for development of resistance, clinicians should screen all patients for acute as well as established HIV infection before prescribing TDF/emtricitabine for PrEP. Specifically, clinicians should take a careful sexual history and screen for symptoms of acute HIV infection, which include fever, rash, pharyngitis, and lymphadenopathy. If acute HIV is suspected based on history, an HIV quantitative nucleic acid amplification test should be obtained to test for acute HIV infection.51 The fourth-generation HIV antibody/antigen test should be used to evaluate whether patients are infected with HIV before PrEP is prescribed. The fourth-generation test is preferred because the addition of antigen testing shortens the window period by 3 to 5 days and therefore will detect patients with early HIV infection who would otherwise be missed.51 Within the first 10 days after very recent HIV infection, known as the “eclipse period,” results of both nucleic acid testing and the antibody/antigen test may be falsely negative. Therefore, if hyperacute infection is suspected, repeated testing should be performed before initiating PrEP.

Future PrEP Strategies
Daily oral TDF/emtricitabine was the first formulation developed for antiretroviral chemoprophylaxis, but other strategies will likely follow. An intravaginal ring containing dapivirine, a nonnucleoside reverse transcriptase inhibitor, decreased HIV incidence in African women with placebo (P = .04)52 and is now undergoing further evaluation. An injectable, long-acting integrase strand transfer inhibitor, cabotegravir, is safe and well-tolerated,53 and 2 large efficacy trials are under way in MSM and transgender people and in African women, evaluating dosing every 8 weeks after initial loading. Another novel approach to prevent HIV acquisition is via immunoprophylaxis using broadly neutralizing monoclonal antibodies (bnAbs), neutralizing antibodies that inhibit the replication of more than 1 strain of HIV. VRC01 is a bnAb that has been found to be safe and well-tolerated after multiple intravenous administrations54 and is currently being evaluated in 2 large efficacy trials in MSM and transgender people in the Americas and women in sub-Saharan Africa.55 Next-generation bnAbs with greater potency and broader range of antiviral activities are in early-phase studies and could result in 1 or more products that could be used clinically.56 Studies are under way to evaluate the use of implanted and transdermal antiretrovirals for prevention, which may provide chemoprophylactic regimens that could be administered every few months.57,58 Much like hormonal contraception, the development of additional PrEP prescription options will be important, since some individuals may prefer the convenience of less frequent dosing regimens, while others may prefer the safety profile of one approach vs another. However, in the near term, oral TDF/emtricitabine is the only available PrEP modality.

Conclusions
Reducing HIV transmission remains a major public health goal. Rates of HIV transmission have declined modestly in the United States, but additional new cases of HIV infection can be prevented with more frequent use of PrEP. The safety and efficacy of TDF/emtricitabine for PrEP has been demonstrated since it was first approved for use in 2012. Primary care clinicians should routinely obtain sexual and drug use histories from their patients and offer PrEP to MSM and heterosexuals who do not consistently use condoms with HIV-infected partners or who have multiple partners and to intravenous drug users who share injection equipment.32 When counseling patients regarding the risks and benefits of PrEP, clinicians should emphasize that when taken consistently, TDF/emtricitabine is effective at preventing HIV infection.59 However, TDF/emtricitabine does not protect against other STIs; hence, the continued importance of condom use.

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Critical revision of the manuscript for important intellectual content: Mayer. Supervision: Riddell.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Edward Livingston, MD, at edward.livingston@ianetwork.org or Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

REFERENCES


