HIV Preexposure Prophylaxis (PrEP)

This is a PDF version of the following document:
Module 5: Prevention of HIV
Lesson 5: HIV Preexposure Prophylaxis (PrEP)

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Introduction

Background

Despite decades of efforts to implement HIV-related risk-reduction programs in the United States, the number of new HIV infections has remained greater than 30,000 new infections per year (Figure 1).[1,2] Furthermore, significant geographic and demographic differences exist for HIV infection rates within the United States HIV epidemic, with the bulk of new infections occurring among young men who have sex with men (MSM), with particularly high rates among Black and Hispanic men in the South.[2,3] It is clear that additional efforts are needed to reduce the number of new HIV infections in the United States. The risk of an individual acquiring HIV may fluctuate between periods of high sexual or drug risk activity and periods of low or no risk. Thus, HIV prevention strategies must offer options that are tailored to an individual's needs.[4] An expanding number of HIV prevention methods are being implemented worldwide, and HIV preexposure prophylaxis (PrEP) is now accepted as an important prevention strategy.[4,5] The expanded use of HIV PrEP is a major component in the national initiative—Ending the HIV Epidemic: A Plan for the United States.[6]

Principles of HIV PrEP

The concept of using medication prophylaxis to reduce the risk of acquiring an infectious disease is well established, including the use of antiretroviral therapy to prevent perinatal transmission of HIV.[5,7,8] Most often, HIV PrEP is used to prevent sexual transmission of HIV. In the absence of HIV PrEP, sexual transmission of HIV can occur as HIV crosses the mucosal surfaces to infect susceptible cells. After taking oral daily HIV PrEP or receiving injections of cabotegravir, the cells near the genital mucosal surface achieve high intracellular concentrations of the active components of the antiretroviral medications and thereby block replication of HIV following sexual contact with a person who has HIV.(Figure 2)

Types of HIV PrEP

There are now three fundamental types of HIV PrEP that are used in the United States: (1) daily oral HIV PrEP with either oral tenofovir DF-emtricitabine or oral tenofovir alafenamide-emtricitabine, (2) on-demand (2-1-1) dosing using oral tenofovir DF-emtricitabine, and (3) injectable HIV PrEP (using long-acting injectable cabotegravir).[9] (Figure 3)

Guidelines for HIV PrEP

- **Centers for Disease Control and Prevention (CDC)**: In December 2021, the Centers for Disease Control and Prevention (CDC) and the U.S. Public Health Service (USPHS) published an updated 2021

CDC PrEP Clinical Practice Guideline along with an updated Clinical Providers' Supplement.[9,10]

- **International Antiviral Society-USA (IAS-USA)**: In December 2022, the International Antiviral Society-USA Panel (IAS-USA) updated the Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults guidelines, which include recommendations for prescribing oral and injectable HIV PrEP.[11]
- **United States Preventive Services Task Force (USPSTF)**: In August 2023, the United States Preventive Services Task Force (USPSTF) gave a Grade A recommendation for the use of HIV PrEP by clinicians to reduce HIV acquisition in persons at risk of acquiring HIV.[12,13]

Persons to Consider for HIV PrEP

In the United States, it is estimated that approximately 1.2 million persons have an HIV PrEP indication.[9,14] Although use of HIV PrEP has increased in the United States in recent years, data from 2022 indicate that only 26% of individuals in the United States with an HIV PrEP indication were prescribed HIV PrEP (Figure 4).[15,16] In addition, significant differences in access to and receipt of HIV PrEP persist based on socioeconomic and demographic factors, such as region of residence, sex, age, race, ethnicity, insurance status, residing in a state with expanded Medicaid or an HIV PrEP drug assistance program, as well as other factors.

Screening for HIV PrEP

Health care professionals should provide all sexually active adult and adolescent persons with information regarding HIV PrEP.[9] A brief sexual history is recommended to assess the risk of acquiring HIV and potential indications for HIV PrEP. The specific indications for HIV PrEP, as recommended in the 2021 CDC PrEP Clinical Practice Guideline, are outlined as follows:

Sexually Active Adults and Adolescents who Weigh at Least 35 kg

Anal or vaginal sex in past 6 months AND any of the following:

- Sex partner with HIV (especially if the person with HIV has an unknown or detectable viral load)
- Bacterial sexually transmitted infection within the past 6 months (gonorrhea, chlamydia, and syphilis for MSM, including those who inject drugs; gonorrhea and syphilis for heterosexual women and men, including persons who inject drugs)
- History of inconsistent or no condom use with sexual partner(s)

Persons who Inject Drugs

Persons who inject drugs should also be assessed for their sexual risk of HIV.

- Injecting partner who has HIV

or

- Sharing injection equipment

or

- Have sexual risk for acquiring HIV

Recommended Regimens and Dosing for HIV PrEP

Currently, in the United States, there are three medications that have received FDA approval for HIV PrEP: oral tenofovir DF-emtricitabine, oral tenofovir alafenamide-emtricitabine, and long-acting injectable cabotegravir.[17,18]

Tenofovir DF-emtricitabine

- **Data**: Findings from multiple, randomized clinical trials using oral tenofovir DF-emtricitabine as HIV PrEP have demonstrated safety and a substantial reduction in the rate of HIV acquisition for MSM,[19,20,21] men and women in heterosexual HIV-serodifferent couples (one person has HIV and the other does not),[22] heterosexual men and women recruited as individuals,[23] In addition, tenofovir DF alone was shown to be safe and effective as HIV PrEP for persons who inject drugs.[24]
- **FDA Approval and Indication for HIV PrEP**: In July 2012, the FDA approved tenofovir DF-emtricitabine for HIV PrEP.[25] Tenofovir DF-emtricitabine is indicated for HIV PrEP to reduce the risk of sexually-acquired HIV in adults and adolescents (weighing at least 35 kg). Individuals must have a negative HIV test prior to starting tenofovir DF-emtricitabine for HIV PrEP.
- **Dosing**: The recommended dosing of tenofovir DF-emtricitabine when used for HIV PrEP is one tablet once daily. Alternative dosing, such as on-demand (2-1-1) dosing, is not included in the FDA indication but can be considered “off-label” for select MSM, per CDC guidelines.
- **Formulation**: tenofovir DF-emtricitabine is a two-drug, fixed-dose combination that contains 300 mg of tenofovir DF and 200 mg of emtricitabine 200 mg.
- **Food Requirements**: Take with or without food.
- **Use in Persons with Renal Impairment**: Tenofovir DF-emtricitabine is not recommended for HIV PrEP in persons who have an estimated creatinine clearance of less than 60 mL/min.

Tenofovir alafenamide-emtricitabine

- **Data**: In the phase 3 DISCOVER trial, tenofovir alafenamide-emtricitabine was noninferior to tenofovir DF-emtricitabine as HIV PrEP for men who have receptive anal sex.[26]
- **FDA Approval and Indication for HIV PrEP**: In October 2019, the FDA approved tenofovir alafenamide-emtricitabine for HIV PrEP in adults and adolescents (weighing at least 35 kg) who are at risk of acquiring HIV sexually, excluding women at risk from receptive vaginal sex.[27] Tenofovir alafenamide-emtricitabine is not indicated for receptive vaginal sex because effectiveness in this population has not been established, although it is currently under investigation. In addition, tenofovir alafenamide-emtricitabine as HIV PrEP has not yet been adequately studied using on-demand (2-1-1) dosing, or in people who are risk of acquiring HIV from injecting drugs. Individuals must have a negative HIV test prior to starting tenofovir alafenamide-emtricitabine for HIV PrEP.
- **Dosing**: For HIV PrEP, tenofovir alafenamide-emtricitabine should be taken as one tablet once daily. Alternative dosing, such as on-demand (2-1-1) dosing, is not recommended.
- **Formulation**: Tenofovir alafenamide-emtricitabine is a two-drug, fixed-dose combination that contains 25 mg of tenofovir alafenamide and 200 mg of emtricitabine.
- **Food Requirements**: Take with or without food.
- **Use in Persons with Renal Impairment**: For HIV PrEP, tenofovir alafenamide-emtricitabine is not recommended for persons who have an estimated creatinine clearance of less than 30 mL/min, unless they are on dialysis. For those on dialysis, tenofovir alafenamide-emtricitabine should be given after dialysis on the days when dialysis is performed.

Long-Acting Injectable Cabotegravir

- **FDA Approval and Indication for HIV PrEP**: In December 2021, the FDA approved long-acting injectable cabotegravir as HIV PrEP for adults and adolescents (weighing at least 35 kg) who are at risk of sexual acquisition of HIV. Long-acting cabotegravir has not been studied as a prevention

measure for people who are at risk of acquiring HIV from injecting drugs.

- **Dosing**: Long-acting injectable cabotegravir is given as a 600 mg (3 mL) injection, which is repeated 1 month after the first injection, and then repeated every 2 months thereafter. An optional oral lead-in with cabotegravir 30 mg once daily may be used for approximately 1 month to assess the tolerability of cabotegravir. If the oral cabotegravir lead-in is used, the first injection of cabotegravir should be given on the last day of the oral lead-in (or within 3 days of completing the oral lead-in).
- **Formulation**: Cabotegravir is available as a 200 mg/mL solution and is administered as a 3 mL intramuscular injection in the gluteal region. Oral cabotegravir is a 30 mg tablet that is taken once daily.
- **Food Requirements**: Long-acting injectable cabotegravir has no food restrictions. Oral cabotegravir can be taken with or without food.
- **Use in Persons with Renal Impairment**: For HIV PrEP, cabotegravir has no renal restrictions. For persons who have a creatinine clearance less than 30 mL/min, increased monitoring for cabotegravir toxicity is recommended. Hemodialysis is not expected to impact cabotegravir levels.

On-Demand (2-1-1) HIV PrEP

- **On-Demand (2-1-1) HIV PrEP**: The dosing with on-demand (2-1-1) HIV PrEP consists of taking tenofovir DF-emtricitabine before and after sex. This approach to HIV PrEP was shown to be highly efficacious at preventing HIV in MSM in the large IPERGAY trial.[21] Although on-demand dosing is not FDA-approved for HIV PrEP in the United States, the 2021 CDC PrEP Clinical Practice Guideline recommends that on-demand (2-1-1) HIV PrEP with oral tenofovir DF-emtricitabine can be considered in selected adult MSM.[9] A person who starts on-demand HIV PrEP can change to daily dosing or to injectable cabotegravir.
- **Dosing with On-Demand (2-1-1) HIV PrEP**: Dosing with on-demand HIV PrEP consists of taking 2 pills of tenofovir DF-emtricitabine 2 to 24 hours prior to sex, then 1 pill 24 hours after the initial 2 pills, and then 1 pill 48 hours after the initial 2 pills. If sexual activity continues on consecutive days, then 1 pill a day should continue to be taken for 48 hours after the last sexual event.[9] For MSM using demand dosing, clinicians should provide counseling about the importance of taking the doses as recommended for every sexual encounter and about the importance of continuing to have follow-up HIV and STI testing. On-demand HIV PrEP should not be used for persons with chronic hepatitis B infection.

Additional Considerations

- **HIV PrEP for Persons who Inject Drugs**: Although no medication has an FDA indication for preventing HIV acquisition through injection drug use, the Bangkok Tenofovir Study showed that persons who inject drugs and take daily tenofovir DF for HIV PrEP experience a significant reduction in new HIV infections compared with persons taking placebo, with this benefit of PrEP occurring for both men and women.[24] Accordingly, persons who inject drugs should be considered for PrEP with daily tenofovir DF-emtricitabine to prevent acquisition of HIV through injection drug use.[9,28] In addition, persons who inject drugs may also have a risk of sexual acquisition of HIV and, therefore, may have an indication for HIV PrEP separate from injection drug use.[9]
- **Women in Periconception, Antepartum, and Postpartum Periods**: Women are at increased risk of HIV acquisition during the periconception period due to multiple factors.[29,30,31] There are substantial data in women demonstrating the safety of tenofovir DF-emtricitabine for HIV PrEP and for treatment of HIV during the periconception, antepartum, and postpartum periods.[23,32,33] If HIV PrEP is indicated during pregnancy, the recommended regimen is daily oral tenofovir DF-emtricitabine.[34] In addition, if a woman becomes pregnant while taking daily oral tenofovir DF-emtricitabine for HIV PrEP, and the risk of HIV exposure is ongoing, she can continue this medication. Tenofovir alafenamide-emtricitabine is not recommended as HIV PrEP during pregnancy since it is not recommended for prevention of vaginal acquisition of HIV. Although cabotegravir is indicated for use in women, it is not recommended during pregnancy or breastfeeding, due to inadequate data in this

setting.

Baseline Laboratory Evaluation, Immunizations, and Counseling

Baseline Laboratory Studies

The 2021 CDC PrEP Clinical Practice Guideline recommends performing a risk assessment and baseline laboratory evaluation prior to prescribing HIV PrEP.[9] In order to qualify for HIV PrEP, an individual should have substantial, ongoing risk for HIV and a baseline laboratory evaluation that includes the following.[9]

- **HIV Testing**: For persons starting oral HIV PrEP, baseline HIV testing, ideally with a laboratory HIV-1/2 antigen-antibody immunoassay, with reflex HIV-1/2 antibody differentiation assay confirmation, should be performed within 1 week of starting. Alternatively, a point-of-care fingerstick blood test can be performed for the initial HIV screening test. Note that oral point-of-care HIV tests are not recommended for HIV testing prior to starting HIV PrEP due to the low sensitivity of these tests for diagnosing recent HIV infection. For persons starting cabotegravir, HIV testing should also include an HIV RNA test prior to starting oral cabotegravir (if used as a lead-in) and prior to the first injection. Confirming a negative baseline HIV test prior to starting HIV PrEP is extremely important, particularly since use of the two-drug HIV PrEP regimen (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine) or a single agent (cabotegravir) in a person with HIV infection would provide inadequate treatment and likely result in the development of significant HIV drug resistance.
- **Renal Function**: For persons planning to receive either tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine, a baseline serum creatinine should be ordered to evaluate renal function, including a confirmed calculated creatinine clearance using the Cockcroft-Gault formula. Persons with an estimated creatinine clearance less than 60 mL/min should not receive tenofovir DF-emtricitabine for HIV PrEP. Similarly, persons with estimated creatinine clearance less than 30 mL/min should not receive tenofovir alafenamide-emtricitabine for HIV PrEP. Baseline laboratory studies to evaluate renal function are not required for persons starting on injectable cabotegravir (with or without an oral lead-in).
- **Sexually Transmitted Infections**: Baseline testing for sexually transmitted infections should include testing for gonorrhea, chlamydia, and syphilis. Testing for syphilis requires a blood draw. Testing for gonorrhea and chlamydia should utilize nucleic acid testing (NAT) and samples should be obtained from anatomic sites of sexual exposure.
- **Lipid Panel**: Persons who receive tenofovir alafenamide-emtricitabine should have a baseline lipid panel as tenofovir alafenamide-emtricitabine can cause alterations in serum lipids, including elevated triglyceride levels. When tenofovir alafenamide-emtricitabine and tenofovir DF-emtricitabine are compared, lipid parameters are higher with the tenofovir alafenamide option, though whether this is clinically significant remains controversial.
- **Hepatitis B**: For all persons with unknown hepatitis B status, baseline serologic screening should include hepatitis B surface antigen (HBsAg), antibody to hepatitis B core (anti-HBc), and antibody to hepatitis B surface antigen (anti-HBsAg). Persons nonimmune to hepatitis B should be offered immunization for hepatitis B. Persons who have a positive HBsAg test should have further evaluation for the management of hepatitis B. Testing for hepatitis B is important because HIV PrEP medications also treat HBV, and an individual with active hepatitis B infection could develop a hepatitis flare following discontinuation of the HIV PrEP medications.[35] Persons with active hepatitis B can receive HIV PrEP, but upon discontinuation of HIV PrEP, they require close follow-up and evaluation for further management of hepatitis B infection. Furthermore, as of 2023, the CDC recommends that all adults in the United States undergo screening for hepatitis B infection at least one time.[36]
- **Hepatitis C**: For persons who are starting HIV PrEP, baseline screening for hepatitis C virus (HCV) infection should be performed for all MSM and persons who inject drugs. Testing for HCV infection should consist of an initial HCV antibody test, followed by HCV RNA testing for all positive HCV antibody tests. For persons who have never had testing for HCV, a one-time HCV testing is recommended for all adults in the United States who are 18 years of age and older.[37]
- **Pregnancy Testing**: For women of childbearing age who are starting on HIV PrEP, a baseline pregnancy test should be performed.

Immunizations

The evaluation and management of persons receiving HIV PrEP also provides an opportunity to counsel and administer vaccines for pathogens that may be transmitted through sex or injection drug use. Screening for hepatitis B in persons initiating HIV PrEP will identify some persons who are nonimmune to hepatitis B; these individuals should receive a complete hepatitis B vaccine series.[38] In addition, hepatitis A immunization is recommended for certain populations that may overlap with persons seeking HIV PrEP, including MSM and persons who inject drugs.[39] Persons seeking HIV PrEP who have not received the human papillomavirus (HPV) vaccine and are candidates (based on their age) for this vaccine should receive immunization with the 9-valent HPV vaccine.[38,40] Individuals with elevated risk for HIV acquisition might also have an increased risk of acquiring mpox virus and thus would also benefit from vaccination with the mpox vaccine.[41] Screening for potential HIV PrEP use is also an opportunity to review whether a person has received routine, recommended vaccinations and offer immunizations if they have not received recommended immunizations.

Behavioral Risk-Reduction Counseling

Because high medication adherence is critical to HIV PrEP efficacy, but is often not achieved, individuals at risk of acquiring HIV should be encouraged and enabled to use HIV PrEP in combination with other effective HIV prevention methods.[10] When HIV PrEP is prescribed, clinicians should provide access, directly or by facilitated referral, to proven effective risk-reduction and support services.[10] In addition, it is important to counsel persons who take HIV PrEP that HIV PrEP medications do not prevent acquisition of bacterial sexually transmitted infections or infections, such as hepatitis C virus, that can be acquired from sharing injecting needles or other injecting equipment.

Major HIV PrEP Studies

There have been multiple large, randomized, controlled trials investigating the efficacy of HIV PrEP in groups with different risk factors, as summarized below.

Men Who have Anal Sex

- **DISCOVER**: This phase 3, randomized, double-blind trial compared the safety and efficacy of daily oral tenofovir alafenamide-emtricitabine with daily oral tenofovir DF-emtricitabine for HIV PrEP in adult men who have anal sex with other men.[26] The study enrolled a total of 5,387 persons in the United States and Canada.[26] Primary efficacy analysis at week 48 (for all participants) and week 96 (for half of participants) indicated the incidence of documented new HIV infections with daily tenofovir alafenamide-emtricitabine (0.16 per 100 person-years) was noninferior to daily tenofovir DF-emtricitabine (0.34 per 100 person-years) at preventing HIV acquisition.[26]
- **HPTN 083**: The HPTN 083 study was a randomized, double-blind, double-dummy, noninferiority trial to compare long-acting injectable cabotegravir with daily oral tenofovir DF–emtricitabine for the prevention of HIV infection in adults at risk of acquiring HIV (mostly men who have sex with men).[17] The cabotegravir regimen consisted of a 5-week lead-in with oral cabotegravir (30 mg daily), followed by 2 doses of intramuscular cabotegravir (600 mg) 4 weeks apart, followed by injectable cabotegravir every 8 weeks.[17] There were 39 new HIV infections (incidence 1.22 per 100 person-years) in the tenofovir DF-emtricitabine group and 13 infections (incidence 0.41 per 100 person-years) in the cabotegravir arm.[17]
- **IPreX**; The HIV Iniciativa Profilaxis Pre-Exposición (iPrEx) study was a phase 3, randomized, double-blind, placebo-controlled trial conducted in Peru, Ecuador, Brazil, Thailand, South Africa, and the United States that enrolled 2,499 HIV-seronegative adult men who have anal sex with men.[19] Participants were randomly assigned to receive a daily oral dose of tenofovir DF-emtricitabine or placebo. This study documented 44% fewer new HIV infections among those who received daily tenofovir DF-emtricitabine for HIV PrEP when compared to those who received placebo.[19] The reduction in new HIV infections was much higher (92%) when limiting the analysis to participants with detectable levels of study drug (indicating adherence to the medication).[19]
- **IPERGAY**: The ANRS Intervention Préventive de l'Exposition aux Risques avec et pour les Gays (IPERGAY) study was a phase 3, randomized, double-blind, placebo-controlled trial in France and Canada evaluating the efficacy of oral tenofovir DF-emtricitabine taken before and after sexual activity (referred to as intermittent, on-demand, or 2-1-1 dosing) for the prevention of HIV among 400 sexually active adult men who have anal sex with other men.[21] After a median follow-up of 9.3 months, the relative risk reduction in HIV infection was 86% in persons taking on-demand tenofovir DF-emtricitabine arm.[21]
- **PROUD:** The Preexposure Option for Reducing HIV in the UK (PROUD) study was a phase 4, randomized, open-label study at 13 clinics in England that evaluated the efficacy of daily oral tenofovir DF-emtricitabine for the prevention of HIV among sexually active men without HIV who reported condomless anal sex with men in the previous 90 days.[20] The 544 study participants were randomized to receive daily tenofovir DF-emtricitabine either immediately upon enrollment or after a deferral period of 1 year. The relative risk reduction in HIV infection in the immediate arm (participants who took tenofovir DF-emtricitabine daily) was 86%.[20]

Heterosexual Men and Women

- **Partners PrEP**:The Partners PrEP trial was a phase 3, randomized, double-blind, placebo-controlled study that enrolled 4,758 HIV-serodifferent heterosexual couples in Uganda and Kenya to receive daily oral tenofovir DF, daily oral tenofovir DF-emtricitabine, or daily oral placebo for the prevention of HIV acquisition.[22] The partners with HIV had a median CD4 count of 495 cells/mm^3 and were not receiving antiretroviral therapy (because they were not eligible per local treatment guidelines that existed at the time the study was conducted).[22] The trial was stopped after an interim analysis

showed statistically significant lower HIV transmission rates in both the tenofovir DF and tenofovir DF-emtricitabine groups compared with the placebo group; investigators reported a 75% reduction in HIV acquisition among the partners who were HIV-seronegative and taking daily oral tenofovir DF-emtricitabine, and a 67% reduction among those taking only daily oral tenofovir DF.[22]

- **TDF2**: The Botswana TDF2 Trial, a phase 3, randomized, double-blind, placebo-controlled study of the safety and efficacy of daily oral tenofovir DF-emtricitabine, enrolled 1,219 heterosexual men and women in Botswana who had tested negative for HIV.[23] In this study, daily oral use of tenofovir DF-emtricitabine resulted in a 62% reduction in HIV acquisition when compared with placebo.[23] Adherence by pill count was 84% in both medication groups.

Women

- **HPTN 084**: The HPTN 084 study was a phase IIb/3, randomized, double-blind trial to compare long-acting injectable cabotegravir with daily oral tenofovir DF–emtricitabine for the prevention of HIV infection in women at risk for acquiring HIV.[18] The cabotegravir regimen consisted of a 5-week lead-in with oral cabotegravir (30 mg daily), followed by 2 doses of intramuscular cabotegravir (600 mg) 4 weeks apart, followed by injectable cabotegravir every 8 weeks.[18] There were 34 new HIV infections (incidence 1.79 per 100 person-years) in the tenofovir DF-emtricitabine group and 4 infections (incidence 0.21 per 100 person-years) in the cabotegravir arm. Long-acting injectable cabotegravir demonstrated superior efficacy, as compared with tenofovir DF-emtricitabine for the prevention of HIV in women.[18]
- **FEM-PEP**: The FEM-PrEP trial was a phase 3, randomized, double-blind, placebo-controlled study of the HIV prevention efficacy and clinical safety of daily oral tenofovir DF-emtricitabine among heterosexual women in South Africa, Kenya, and Tanzania.[42] Participants were seen at monthly follow-up visits, and the study drug was discontinued among women who became pregnant during the trial.[42] The trial was stopped in 2011 when an interim analysis determined that the trial would be unlikely to detect a statistically significant difference in efficacy between the two study groups.[42] Adherence was low in this trial, with detectable plasma drug levels in less than 50% of the women assigned to tenofovir DF-emtricitabine.[42]
- **VOICE**: The Vaginal and Oral Interventions to Control the Epidemic (VOICE) study was a randomized, placebo-controlled trial that enrolled women of reproductive age and randomized them to one of three HIV preventative medications (oral tenofovir DF-emtricitabine daily, oral tenofovir DF daily, or a 1% tenofovir vaginal gel) versus placebo.[43] A total 5,029 participants were enrolled at 15 sites in South Africa, Uganda, and Zimbabwe.[43] None of the study arms were found to be effective at reducing the likelihood of HIV transmission as compared to placebo, but adherence to the study drugs was documented to be low.[43]

People who Inject Drugs (PWID)

- Bangkok Tenofovir Study (BTS): The Bangkok Tenofovir Study (BTS) was a phase 2/3, CDC-sponsored, double-blind, placebo-controlled trial that randomized 2,713 persons without HIV who inject drugs to receive either daily oral tenofovir DF or placebo.[24] All participants also received access to addiction support services, methadone programs, bleach for cleaning needles, condoms, and primary care medical services.[24] After a median follow-up time of 4.6 years, the relative risk reduction in HIV was 49% among study participants in the tenofovir DF arm; the relative risk reduction was 70% in a subgroup analysis of individuals with detectable plasma tenofovir levels.[24]

Time to Achieve Protection after Initiating HIV PrEP

After initiating oral HIV PrEP with tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine, these medications must reach the body tissues and then undergo phosphorylation to function as inhibitors of HIV replication. Available data in humans suggest that with oral ingestion of tenofovir DF, the maximal concentrations of tenofovir diphosphate (the active form of tenofovir) are obtained in peripheral blood mononuclear cells in about 7 days, rectal tissues at about 7 days, and cervicovaginal tissues at about 20 days.[44,45,46] Similar data for tenofovir alafenamide or cabotegravir are not known. Furthermore, there is no consensus as to the required time to reach protective levels (as opposed to maximum levels). The 2021 CDC PrEP Clinical Practice Guideline does not provide a specific recommendation for the time needed for tenofovir DF-emtricitabine to reach adequate tissue levels to achieve protection from HIV infection.[47] The IAS-USA HIV 2022 Guidelines suggest using a 7-day lead-in time with daily dosing of tenofovir DF-emtricitabine for rectal, penile, and vaginal exposures to ensure adequate tissue levels are achieved, and these guidelines comment that for men starting with a double-dose of tenofovir DF-emtricitabine on the first day likely leads to protective levels by 24 hours (extrapolating data from the 2-1-1 studies).[11] There are no guidelines regarding how long it would take to achieve protection against HIV acquisition after initiating injectable cabotegravir for HIV PrEP. The IAS-USA HIV 2022 Guidelines comment that onset of HIV protection is likely to be approximately 7 days after the first cabotegravir injection, but further research is needed to confirm this estimate.[11]

Impact of Adherence on Efficacy of HIV PrEP

In the HIV PrEP trials completed to date, adherence to HIV PrEP has been the single most important factor that impacts efficacy.[4,48,49] The correlation of adherence with oral HIV PrEP efficacy has been strongest when adherence estimates are based on detection of tenofovir in blood samples (Figure 5).[50] For example, in the iPrEx trial, investigators measured intracellular levels of tenofovir diphosphate and emtricitabine triphosphate and found substantially higher intracellular drug levels in participants who did not acquire HIV than in those subjects who acquired HIV during the study.[19] In the Partners PrEP trial, there was an overall 75% relative reduction in HIV acquisition for persons who received tenofovir DF-emtricitabine compared with those who received placebo; among participants receiving tenofovir DF-emtricitabine who had a detectable blood level of tenofovir (a marker of adherence), there was a 90% reduction in HIV acquisition compared with those with an undetectable tenofovir level.[22]. Similarly, poor adherence has correlated with a lack of HIV PrEP benefit as shown in the FEM-PrEP and VOICE trials.[42,48] The effectiveness of HIV PrEP outside of clinical trials has been found to be lower than in trials, especially for younger individuals and for persons with added adherence challenges due to certain social determinants of health.[51] Because of the extreme importance of good adherence to achieve high HIV PrEP efficacy, regular adherence counseling is recommended for all persons taking HIV PrEP.[9]

Table 1. **USPHS: Preexposure Prophylaxis for the Prevention of HIV Infection in the United States**

Key Components of Oral HIV PrEP Medication Adherence Counseling

Establish trust and bidirectional communication • Medication dosage and schedule • Management of common side effects • Relationship of adherence to the efficacy of PrEP • Signs and symptoms of acute HIV infection and recommended actions
Support adherence • Tailor daily dose to patient's daily routine • Identify reminders and devices to minimize forgetting doses • Identify and address barriers to adherence • Reinforce benefit relative to uncommon harms
Monitor behavioral adherence in a nonjudgmental manner • Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection • Reinforce success • Identify factors interfering with adherence and plan with patient to address them • Assess side effects and plan how to manage them

Source:

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108. [CDC]

Laboratory Monitoring on HIV PrEP

All individuals taking HIV PrEP should have laboratory monitoring as part of their routine follow-up evaluations, but the specific follow-up differs depending on whether the person is taking tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, or cabotegravir.[9] These follow-up evaluations should take place every 3 months for persons taking oral PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine) and every 2 months for those taking injectable cabotegravir. The 2021 CDC PrEP Clinical Practice Guideline recommends the following regarding laboratory monitoring for persons taking HIV PrEP.[9].

- **HIV Testing**: Repeat HIV testing and evaluation for signs and symptoms of acute HIV infection should be performed at least every 3 months for those persons taking oral PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide) and every 2 months for those taking long-acting injectable cabotegravir; in addition, persons receiving cabotegravir should have HIV testing performed 1 month after the first injection. The recommended HIV testing should include both an HIV-1/2 antigen-antibody test and an HIV-1 RNA assay (qualitative or quantitative). The rationale for including HIV-1 RNA in routine testing is that recent data have shown a less than optimal performance with standard HIV-1/2 antigen-antibody testing in persons who acquire HIV while taking antiretroviral medications. That said, if cost or coverage issues prevent the ability to order an HIV RNA test and a person has an indication for HIV PrEP, most experts would prescribe HIV PrEP and perform the best available test for HIV screening. In other words, the inability to access regular HIV RNA testing should not preclude HIV PrEP if a person has a strong indication.

- **Monitoring Renal Function**: Monitoring for renal function should be performed for all persons receiving oral PrEP. Renal function should be assessed every 6 months if the individual is 50 years of age and older, or they have a baseline estimated creatinine clearance of less than 90 mL/min. Persons who are younger than 50 years of age and who have a baseline estimated creatinine clearance of at least 90 mL/min should have renal monitoring every 12 months. Monitoring of renal function is not necessary for persons receiving injectable cabotegravir.

- **Lipid Panel and Weight Monitoring**: Persons receiving tenofovir-alafenamide should have monitoring every 12 months for cholesterol levels, triglyceride levels, and weight.
- **Hepatitis C Serology**: Repeat hepatitis C serologic testing should be performed every 12 months for MSM and persons who inject drugs.
- **Sexually Transmitted Infections (STIs)**: For MSM, screening for bacterial STIs (chlamydia, gonorrhea, and syphilis) should occur at least every 3 months if taking oral HIV PrEP and at least every 4 months if receiving injectable cabotegravir. For heterosexually active women and men who are taking oral HIV PrEP or receiving injectable cabotegravir, screening for syphilis and gonorrhea should occur every 6 months and screening for chlamydia every 12 months. Screening for chlamydia and gonorrhea should use NAAT and include all appropriate body sites based on reported sexual activity.
- **Pregnancy Testing**: For women who might become pregnant while taking HIV PrEP, pregnancy testing should be performed at least every 3 months. If a woman becomes pregnant (or is breastfeeding) while taking HV PrEP, the clinician prescribing HIV PrEP should have a discussion with the woman and their prenatal medical provider about the risks and benefits of continuing HIV PrEP during pregnancy.

Acquisition of HIV in the Setting of HIV PrEP

If HIV infection is documented at the baseline evaluation or via a follow-up evaluation, then a number of subsequent steps should occur.[9]

- **Laboratory Studies**: In persons newly diagnosed with HIV, laboratory studies should be ordered that include a quantitative HIV RNA level (if not already performed as part of the diagnostic evaluation), a CD4 cell count, and an HIV genotype resistance assay (if the HIV RNA level is high enough to perform the genotype, which typically means higher than 200 to 500 copies/mL). If an individual is taking or has taken long-acting injectable cabotegravir for HIV PrEP and acquires HIV, the HIV genotypic resistance testing should include testing integrase resistance assay (this integrase genotype typically requires a separate order from the standard genotype).[52]
- **Initiating Antiretroviral Treatment Regimen**: Once a diagnosis of HIV is made, it is important to start a fully suppressive HIV regimen (if the diagnosis is at the baseline evaluation) or convert the HIV PrEP regimen to a full antiretroviral treatment regimen if the person is receiving or recently received HIV PrEP.[10] If needed, the antiretroviral regimen can be modified when the results from the genotype become available.[53] In general, if a person acquires HIV and has current or recent exposure to oral PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine), the change to antiretroviral treatment should involve the addition of a potent integrase inhibitor (by adding dolutegravir to the tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine or by prescribing bictegravir-tenofovir alafenamide-emtricitabine).[53] On the other hand, if a person acquires HIV and has had exposure to injectable cabotegravir, the recommended initial antiretroviral therapy regimen is boosted darunavir plus tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine. The boosted darunavir can be switched to an integrase inhibitor if the integrase genotype confirms no resistance.[53]
- **Provide or Link to HIV Treatment Services**: If the clinician prescribing PrEP is not experienced with HIV management and antiretroviral therapy, then the person newly diagnosed with HIV should receive a referral to a medical provider who has significant HIV clinical treatment expertise.
- **Counseling and Partner Notification**: The person newly diagnosed with HIV should receive counseling about their HIV status and steps they should take to prevent HIV transmission to others. Partner notification should occur with all persons newly diagnosed with HIV.

HIV PrEP and Development of HIV Drug Resistance

HIV Drug Resistance in Persons Taking HIV PrEP

Although development of drug resistance is a concern for an individual who acquires HIV while taking tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, or injectable cabotegravir, large HIV PrEP trials have reported low rates of developing HIV resistance when taking HIV PrEP.[17,22,54,55] In the iPrEx study, only 2 of the 48 persons taking tenofovir DF-emtricitabine who acquired HIV showed resistance mutations, and these minor variant mutations (e.g., M184I) were detected only with deep sequencing.[54] In the Partners PrEP study, 5 of 63 (7.9%) seroconverters in the active HIV PrEP arms of the study developed HIV drug resistance, and resistance was more common in persons assigned to the tenofovir DF-emtricitabine arm compared with the tenofovir DF only arm.[55] In the cabotegravir HPTN 083 study, resistance to integrase strand transfer inhibitors was documented in 4 of 9 breakthrough infections among persons in the cabotegravir arm; reverse-transcriptase inhibitor mutations (K65R, M184V, M184I) were observed in 4 persons who had breakthrough HIV infections while taking tenofovir DF-emtricitabine.[17] Taken together, available data suggest that HIV PrEP-related HIV drug resistance in persons taking HIV PrEP will occur at a low rate as long as HIV infection is ruled out prior to starting HIV PrEP and persons taking HIV PrEP have regular HIV testing.

Evaluation for Suspected HIV Drug Resistance

An HIV RNA level and an HIV genotype resistance assay should be ordered promptly for any person taking HIV PrEP who is diagnosed with HIV.[9] In some instances, however, individuals who acquire HIV while taking HIV PrEP may have detectable HIV RNA but at a level below the range for reliable performance of HIV genotyping. This scenario occurs because HIV PrEP medications will only partially suppress viral replication. In this setting, the role of HIV DNA genotyping (also known as a proviral genotype), which can be performed with very low or undetectable HIV RNA levels, has not been clearly defined. If a person acquires HIV while taking oral HIV PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine) or with recent exposure to oral HIV PrEP, the baseline genotype upon diagnosis of HIV can be a standard genotype that assesses for mutations in the reverse transcriptase and protease genes (the primary purpose is to assess for mutations that would compromise the NRTI backbone of a treatment regimen). If, however, a person acquires HIV and has previously received injectable cabotegravir, regardless of the time since last injection or since drug discontinuation (because the drug has a very long half-life), the baseline genotype should also include a check for resistance-associated mutations in the integrase gene (to assess for mutations that would affect the anti-HIV activity of the integrase inhibitor mutations). Depending on the lab, this may require a separate order.

Monitoring for HIV Infection to Prevent Resistance

Baseline HIV testing prior to starting HIV PrEP is essential to make sure an individual with HIV does not start taking a regimen that would be inadequate for HIV and that would lead to the rapid development of drug resistance. For persons taking HIV PrEP, regular HIV testing is extremely important to minimize the duration of exposure to medications if they acquire HIV while taking HIV PrEP. Furthermore, to minimize the risk of developing resistance among persons taking oral HIV PrEP, the 2021 CDC PrEP Clinical Practice Guideline recommends prescribing no more than 90 days of medication at a time and repeating HIV testing every 3 months.[9] For MSM receiving on-demand (2-1-1) HIV PrEP with tenofovir DF-emtricitabine, a maximum of 30 pills should be provided before repeat HIV testing is performed, which would provide adequate medication for 7 exposure events.[9] Individuals taking injectable cabotegravir should have HIV testing at the time of the initial 1-month injection visit and then every 2 months thereafter (following the same schedule as the injections).[9] The recommended HIV testing for persons receiving oral HIV PrEP or injectable cabotegravir should include both an HIV-1/2 antigen-antibody assay and HIV-1 RNA testing.[9] Any person who develops symptoms consistent with acute HIV should also have HIV testing, including an HIV RNA assay.[9]

Adverse Effects of Medications Used for HIV PrEP

Adverse Effects with Tenofovir DF-Emtricitabine

In several large studies in which tenofovir DF-emtricitabine was used for HIV PrEP, the medication was well tolerated and safe. The most common side effects reported in the HIV PrEP studies were nausea and decreased appetite, primarily occurring in the first month of taking the drug (sometimes referred to as “start-up syndrome”).[5,47] These side effects led to mild weight loss in some subjects, which generally stabilized after the first month. Tenofovir DF can cause renal dysfunction, specifically proximal tubulopathy, but renal adverse events in large trials of HIV PrEP were either similar to or only slightly more common than with placebo, and resolved with discontinuation of the medication.[56,57,58] Nevertheless, extensive treatment experience with tenofovir DF when used as treatment for persons with HIV infection has shown the potential for tenofovir DF to cause nephrotoxicity. Therefore, monitoring of renal function is recommended in all persons taking tenofovir DF-emtricitabine for HIV PrEP.[47] Concern also exists regarding the effects of tenofovir DF on bone mineral density. Toxicity data from HIV PrEP studies have demonstrated a small and clinically insignificant decrease in bone mineral density in participants who took tenofovir DF-emtricitabine.[59,60,61,62] Findings from a recent study suggested the minor losses in bone mineral density that occurred in persons receiving HIV PrEP were recovered within 12 to 18 months after stopping PrEP.[63] Although tenofovir DF could potentially impact bone density, routine baseline (or follow-up) bone density scanning is not considered necessary. For a person who has documented osteoporosis or osteopenia or risk factors for such, some experts would opt for alternate HIV PrEP options if possible.

Adverse Effects with Tenofovir alafenamide-Emtricitabine

In most persons, tenofovir alafenamide-emtricitabine is well tolerated and safe, with better bone and renal safety outcomes than tenofovir DF-emtricitabine.[26] Non-specific “start-up syndrome” symptoms may occur for some individuals, similar to symptoms that may occur with tenofovir DF-emtricitabine. Weight gain, increases in cholesterol, and increases in triglyceride levels have been associated with tenofovir alafenamide-emtricitabine, though the mechanism and long-term consequences are not clear.[9,26].

Adverse Effects with Long-Acting Injectable Cabotegravir

Among persons receiving injectable cabotegravir, the most common adverse effect is injection site reactions, which resulted in the discontinuation of cabotegravir in about 2% of persons receiving this medication.[17] In the cabotegravir HPTN 083 study, among persons who experienced an injection site reaction, the most common symptoms were pain (61%) and tenderness (24%).[17] Injection site reactions typically begin about 1 day after the injection and last about 3 days.[17] Most injection site reactions are mild, self-limited, and do not lead to discontinuation of the medication. Hot or cold packs and as-needed oral analgesics (antiinflammatory medications and acetaminophen) can help to alleviate symptoms.

Changes in Sexual Practices Among Persons Receiving HIV PrEP

Critics of HIV PrEP have argued that its use will lead to behavioral disinhibition and an increase in high-risk sexual and drug use practices.[64,65] Part of this concern was fueled by two meta-analyses that suggested an increased rate of bacterial sexually transmitted infections for MSM taking HIV PrEP, as compared to MSM not taking HIV PrEP.[66,67] In contrast, a systematic review did not find conclusive evidence that taking HIV PrEP leads to an increase in risky sexual activities.[68] The evidence in HIV PrEP clinical trials for risk compensation has been mixed.[22,23,24,64,69,70] At a population level, the impact of risk compensation with HIV PrEP remains unclear. Nevertheless, most experts believe the HIV prevention value of HIV PrEP outweighs any potential change in sexual practices that may occur while persons are receiving HIV PrEP. Individuals prescribed PrEP should always be counseled about other methods for risk reduction, counseled that the medication does not prevent bacterial STIs, and should undergo regular screening for bacterial STIs. Further, dissemination of PrEP can increase the rates of screening, detection, and treatment for STIs, which can be beneficial. [71] Persons receiving HIV PrEP should also be offered doxycycline postexposure prophylaxis (DoxyPEP), which significant reduces the risk of bacterial STIs.[72]

Discontinuing PrEP

There are a number of factors that may lead an individual to discontinue HIV PrEP, including a decline in HIV risk activity, medication-related side effects, or a positive HIV test. In general, HIV PrEP is indicated during periods of substantial risk of acquiring HIV, which may last for months or even years, but it should not typically be viewed as a life-long prevention strategy.[5] Several key factors should be taken into consideration at the time of discontinuing PrEP:[9]

- Upon discontinuation of HIV PrEP, repeat HIV testing should always be performed, and the reason for discontinuing HIV PrEP should be documented in the health record. If, at a later point, an individual wants to restart PrEP, they should undergo the same evaluation as a person newly prescribed HIV PrEP.
- If an individual has chronic HBV infection and discontinues taking HIV PrEP with either tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine, several months of monitoring for a possible HBV flare should occur, or consideration given for the treatment of chronic HBV, if indicated.
- For an individual planning to discontinue oral HIV PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine), the protection from HIV infection will wane within several days after stopping the medication.
- Special consideration needs to be given when injectable cabotegravir is discontinued, since levels of the medication may remain in tissues for a year or longer (up to 4 years in some individuals).[73] If a person discontinues injectable cabotegravir but has an ongoing risk for HIV acquisition, oral HIV PrEP should be recommended as a high priority during the cabotegravir “tail period,” which can last 1 year or longer. In this setting, the oral HIV PrEP (tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine) should be prescribed within 2 months of the last cabotegravir dose. In addition, all persons stopping cabotegravir should have quarterly follow-up visits that include HIV testing for at least 12 months after the last injection of cabotegravir.
- If the individual discontinues HIV PrEP for any reason other than acquiring HIV, they should continue to have HIV testing performed, linkage to HIV prevention support services, and continued risk-reduction counseling.

Transitioning from Nonoccupational HIV PEP to HIV PrEP

Indications for Transition from Nonoccupational HIV PEP to HIV PrEP

All persons who receive one or more courses of HIV nonoccupational postexposure prophylaxis (PEP) and have ongoing or anticipated near-future risk of acquiring HIV should be considered for HIV PrEP. For persons with repeated exposures to HIV, the use of HIV PrEP is preferable to repeated courses of nonoccupational PEP.[9] At the initial visit for persons undergoing evaluation for nonoccupational PEP, the discussion should include information regarding potential transition to HIV PrEP after completing the 28-day course of nonoccupational HIV PEP.

Timing of the Transition from Nonoccupational HIV PEP to HIV PrEP

For persons receiving nonoccupational HIV PEP who are candidates to receive HIV PrEP, the transition from nonoccupational HIV PEP to HIV PrEP should occur without any gap in protection for HIV infection (i.e., the transition should be immediate from the completion of 28 days of HIV PEP to initiation of HIV PrEP on the subsequent day).[9,10,74] The major concern with immediate transition to HIV PrEP is that an individual could have acquired HIV from the exposure that warranted receipt of nonoccupational HIV PEP. If this occurred, the potential for development of HIV resistance would be significant because the individual would be transitioning from nonoccupational PEP (a three-drug regimen) to HIV PrEP (a 2-drug oral regimen or a 1-drug injectable cabotegravir regimen). This risk, however, appears to be very low, especially if adherence is good with occupational HIV PEP and if baseline HIV testing is performed prior to the actual transition.

Evaluation when Transitioning from Nonoccupational HIV PEP to HIV PrEP

The following clinical and laboratory evaluation is recommended when transitioning an individual immediately from nonoccupational HIV PEP to HIV PrEP.[9,10] This transition requires some logistical considerations to ensure the individual begins HIV PrEP immediately upon completing the 28-day nonoccupational PEP regimen.[9,10]

- For persons who are candidates for transition from nonoccupational HIV PEP to HIV PrEP, a follow-up visit will be needed at the completion of the 28-day nonoccupational HIV PEP regimen (or several days prior to completing the regimen). To ensure no gap in HIV protection occurs, it is important the visit does not take place on a date after completion of the 28-day course of nonoccupational HIV PEP.
- At this follow-up visit, the individual should have an assessment for any signs or symptoms that would suggest acute HIV. If an individual is presenting with an illness consistent with acute HIV, then HIV PrEP should be deferred while evaluation of acute HIV is undertaken, and this evaluation should include HIV RNA testing.
- Repeat HIV testing should be performed at this visit, ideally with a laboratory-based HIV-1/2 antigen-antibody immunoassay and an HIV RNA-1 assay. These assays typically require 1-3 days before results are available, which practically means they should be ordered several days prior to the end of the 28-day nonoccupational PEP course, or the person can transition to HIV PrEP at the 28-day visit while the results are pending, with the plan to immediately convert the HIV PrEP to HIV treatment if the HIV testing reveals HIV infection.
- At this visit, individuals transitioning to HIV PrEP should receive counseling about HIV PrEP, and baseline laboratory studies that are indicated should be obtained. The medication regimen can transition from the 3-drug nonoccupational PEP to any of the three HIV PrEP regimens (tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, or long-acting injectable cabotegravir), as long as they are indicated for the individual.
- If HIV testing at any point prior to starting HIV PrEP (or while on HIV PrEP) confirms HIV infection, the individual will need prompt evaluation for the management of newly acquired HIV.

HIV PrEP Uptake

Despite the overwhelming evidence favoring PrEP use for HIV prevention, there are substantial data demonstrating low rates of HIV PrEP uptake among persons who could benefit from taking HIV PrEP in certain demographic groups, particularly (1) Black and Hispanic men who have sex with men and (2) women.[14,75,76,77,78,79,80]

- **HIV PrEP Uptake by Sex:** Recent surveillance data from the CDC for 2021 indicate that among persons at risk for acquiring HIV, 34% of men who could benefit from HIV PrEP were prescribed HIV PrEP compared to 12% among women.[15] A large study in the United States that evaluated HIV-seronegative, nonpregnant women who were 15 to 64 years of age found that HIV PrEP prescription rates were less than 0.5% for women who underwent HIV testing for HIV.[81] In this same study, the investigators also reported that HIV PrEP was not prescribed for more than 13,000 women who were diagnosed with gonorrhea or syphilis.[81] A retrospective analysis following 13,906 insured persons who were prescribed HIV PrEP in a large United States health care system found women, when compared with men, were less likely to receive and initiate HIV PrEP and more likely to discontinue HIV PrEP once it was started.[82]
- **HIV PrEP Update by Race**: Among persons with an HIV PrEP indication, the highest percentage of persons prescribed HIV PrEP was in White people (78%), which was a markedly higher percentage than in Hispanic people (21%) and in Black people (11%).[15] The reasons for these differences are complicated and likely involve many factors, including access to care.
- **HIV PrEP Update by Age**: Among persons in different age groups, persons 16-24 years of age had the lowest percentage of persons with an HIV PrEP indication who had HIV PrEP prescribed for them.[15]

Future HIV PrEP Medications

Further studies are underway to investigate different delivery systems for HIV PrEP as well as different active antiretroviral agents. Some of these novel HIV PrEP strategies that are not FDA-approved in the United States for HIV PrEP include oral or injectable lenacapavir (a capsid inhibitor) and oral or injectable islatravir (a nucleoside reverse transcriptase translocation inhibitor).[83,84] Novel delivery systems, such as microarray patches, vaginal films, implants (including ultra long-acting, refillable implants), and others, are also in development.[85] Lenacapavir has shown remarkable efficacy in women and in MSM.[86,87] Lenacapavir is highly likely to receive FDA approval for HIV PrEP in the United States in 2025. There has been strong development and global interest in the dapivirine vaginal ring, but the dapivirine application for FDA approval in the United States has been withdrawn, but other vaginal rings are in development.[88,89] The future for HIV PrEP medications is likely to include a greater array of medication and delivery system options.

Summary Points

- HIV PrEP has been shown to be a safe and effective HIV prevention option for individuals at substantial risk of acquiring HIV.
- The FDA-approved and recommended HIV PrEP regimens are oral tenofovir DF-emtricitabine, oral tenofovir alafenamide-emtricitabine, and long-acting injectable cabotegravir. Note that tenofovir alafenamide-emtricitabine is not indicated for women or other individuals whose risk factor for HIV acquisition is receptive vaginal sex.
- A risk assessment and baseline laboratory evaluation is required prior to prescribing HIV PrEP, including documentation that the person to receive HIV PrEP has a negative baseline HIV test.
- Monitoring for persons receiving oral HIV PrEP should include HIV testing (HIV-1/2 antigen-antibody testing plus an HIV-1 RNA assay) every 3 months for those on oral medications and every 2 months while receiving long-acting injectable cabotegravir. Regular screening for STIs should occur in all persons receiving HIV PrEP.
- For persons receiving oral HIV PrEP with tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine, renal monitoring should occur every 6 or 12 months, depending on the individual's age and baseline estimated CrCl.
- Adherence to HIV PrEP medications has been the single most important factor that impacts efficacy in the HIV PrEP clinical trials.
- The risk of developing HIV drug resistance associated with HIV PrEP use appears to be low, as long as HIV infection is recognized promptly and the HIV PrEP regimen is converted to a fully suppressive antiretroviral treatment regimen.
- If an individual with chronic hepatitis B infection is taking HIV PrEP, discontinuing tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine could lead to a serious hepatitis B flare.
- Transitioning from nonoccupational HIV PEP to HIV PrEP optimally involves an immediate transition without a gap.
- When discontinuing HIV PrEP, repeat HIV testing should always be performed, and the reason for discontinuation should be documented in the health record.

Citations

1. Song R, Hall HI, Green TA, Szwarcwald CL, Pantazis N. Using CD4 Data to Estimate HIV Incidence, Prevalence, and Percent of Undiagnosed Infections in the United States. J Acquir Immune Defic Syndr. 2017;74:3-9.
[PubMed Abstract] -

2. Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.
[CDC] -

3. Centers for Disease Control and Prevention. HIV Infection, Risk, Prevention, and Testing Behaviors Among Men Who Have Sex With Men—National HIV Behavioral Surveillance, 23 U.S. Cities, 2017. HIV Surveillance Special Report 22:1-30. Published February 2019.
[CDC] -

4. Baeten JM, Heffron R. Pre-exposure prophylaxis to intensify the fight against HIV. Lancet Infect Dis. 2014;14:443-5.
[PubMed Abstract] -

5. Baeten JM, Haberer JE, Liu AY, Sista N. Preexposure prophylaxis for HIV prevention: where have we been and where are we going? J Acquir Immune Defic Syndr. 2013;63 Suppl 2:S122-9.
[PubMed Abstract] -

6. Fauci AS, Redfield RR, Sigounas G, Weahkee MD, Giroir BP. Ending the HIV Epidemic: A Plan for the United States. JAMA. 2019;321:844-845.
[PubMed Abstract] -

7. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. N Engl J Med. 1994;331:1173-80.
[PubMed Abstract] -

8. Chasela CS, Hudgens MG, Jamieson DJ, et al. Maternal or infant antiretroviral drugs to reduce HIV-1 transmission. N Engl J Med. 2010;362:2271-81.
[PubMed Abstract] -

9. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108.
[CDC] -

10. Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: clinical providers' supplement. December 2021:1-53.
[CDC] -

11. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2022 Recommendations of the International Antiviral Society-USA Panel. JAMA. 2023;329:63-84.
[PubMed Abstract] -

12. Chou R, Spencer H, Bougatsos C, Blazina I, Ahmed A, Selph S. Preexposure Prophylaxis for the

Prevention of HIV: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2023;330:746-63.
[PubMed Abstract] -

13. US Preventive Services Task Force; Barry MJ, Nicholson WK, Silverstein M, et al. Preexposure Prophylaxis to Prevent Acquisition of HIV: US Preventive Services Task Force Recommendation Statement. JAMA. 2023;330:736-45.
[PubMed Abstract] -

14. Smith DK, Van Handel M, Wolitski RJ, et al. Vital Signs: Estimated Percentages and Numbers of Adults with Indications for Preexposure Prophylaxis to Prevent HIV Acquisition--United States, 2015. MMWR Morb Mortal Wkly Rep. 2015;64:1291-5.
[PubMed Abstract] -

15. Centers for Disease Control and Prevention. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data—United States and 6 Dependent Areas, 2021. HIV Surveillance Supplemental Report. 2023;28(No. 4). Published May 2023.
[CDC] -

16. U.S. Health and Human Services. America's HIV Epidemic Analysis Dashboard (AHEAD). PrEP Coverage.
[AHEAD] -

17. Landovitz RJ, Donnell D, Clement ME, et al. N Engl J Med. 2021;385:595-608.
[PubMed Abstract] -

18. Delany-Moretlwe S, Hughes JP, Bock P, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. Lancet. 2022;399:1779–89.
[PubMed Abstract] -

19. 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;363:2587-99.
[PubMed Abstract] -

20. 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;387:53-60.
[PubMed Abstract] -

21. Molina JM, Capitant C, Spire B, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med. 2015;373:2237-46.
[PubMed Abstract] -

22. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med. 2012;367:399-410.
[PubMed Abstract] -

23. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med. 2012;367:423-34.
[PubMed Abstract] -

24. 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;381:2083-90.

[PubMed Abstract] -

25. U.S. Department of Health and Human Services and U.S. Food and Drug Administration. Truvada for PrEP Fact Sheet: Ensuring Safe and Proper Use. July 2012
[FDA] -

26. Mayer KH, Molina JM, Thompson MA, et al. Emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial. Lancet. 2020;396:239-54.
[PubMed Abstract] -

27. U.S. Food and Drug Administration. FDA approves second drug to prevent HIV infection as part of ongoing efforts to end the HIV epidemic. October 3, 2019
[U.S. FDA] -

28. US Preventive Services Task Force, Owens DK, Davidson KW, et al. Preexposure Prophylaxis for the Prevention of HIV Infection: US Preventive Services Task Force Recommendation Statement. JAMA. 2019;321:2203-13.
[PubMed Abstract] -

29. Brubaker SG, Bukusi EA, Odoyo J, Achando J, Okumu A, Cohen CR. Pregnancy and HIV transmission among HIV-discordant couples in a clinical trial in Kisumu, Kenya. HIV Med. 2011;12:316-21.
[PubMed Abstract] -

30. Hapgood JP, Kaushic C, Hel Z. Hormonal Contraception and HIV-1 Acquisition: Biological Mechanisms. Endocr Rev. 2018;39:36-78.
[PubMed Abstract] -

31. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. AIDS. 2011;25:1887-95.
[PubMed Abstract] -

32. Heffron R, Ngure K, Velloza J, et al. Implementation of a comprehensive safer conception intervention for HIV-serodiscordant couples in Kenya: uptake, use and effectiveness. J Int AIDS Soc. 2019;22:e25261.
[PubMed Abstract] -

33. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. AIDS. 2017;31:213-232.
[PubMed Abstract] -

34. Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission. Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States. Pre-exposure Prophylaxis (PrEP) to Prevent HIV During Periconception, Antepartum, and Postpartum Periods. December 30, 2021.
[HIV.gov] -

35. Honkoop P, de Man RA, Niesters HG, Zondervan PE, Schalm SW. Acute exacerbation of chronic hepatitis B virus infection after withdrawal of lamivudine therapy. Hepatology. 2000;32:635-9.
[PubMed Abstract] -

36. Conners EE, Panagiotakopoulos L, Hofmeister MG, et al. Screening and Testing for Hepatitis B Virus Infection: CDC Recommendations - United States, 2023. MMWR Recomm Rep. 2023;72:1-25.

[PubMed Abstract] -

37. Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. MMWR Recomm Rep. 2020;69:1-17.
[PubMed Abstract] -

38. Advisory Committee on Immunization Practices (ACIP). Recommended Immunization Schedule for Ages 19 Years or Older, United States, 2025.
[ACIP] -

39. Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR Recomm Rep. 2020;69:1-38.
[PubMed Abstract] -

40. Advisory Committee on Immunization Practices (ACIP). Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024.
[ACIP] -

41. Centers for Disease Control and Prevention (CDC). Mpox Vaccination. Updated December30, 2024
[CDC] -

42. Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2012;367:411-22.
[PubMed Abstract] -

43. Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. N Engl J Med. 2015;372:509-18.
[PubMed Abstract] -

44. 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;3:112re4.
[PubMed Abstract] -

45. Anderson PL, Kiser JJ, Gardner EM, Rower JE, Meditz A, Grant RM. Pharmacological considerations for tenofovir and emtricitabine to prevent HIV infection. J Antimicrob Chemother. 2011;66:240-50.
[PubMed Abstract] -

46. Seifert SM, Glidden DV, Meditz AL, et al. Dose response for starting and stopping HIV preexposure prophylaxis for men who have sex with men. Clin Infect Dis. 2015;60:804-10.
[PubMed Abstract] -

47. US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update. A Clinical Practice Guideline. March 2018:1-77.
[CDC] -

48. Aaron E, Cohan D. Preexposure prophylaxis for the prevention of HIV transmission to women. AIDS. 2013;27:F1-5.
[PubMed Abstract] -

49. Sivay MV, Li M, Piwowar-Manning E, et al. Characterization of HIV Seroconverters in a TDF/FTC PrEP Study: HPTN 067/ADAPT. J Acquir Immune Defic Syndr. 2017;75:271-9.
[PubMed Abstract] -

50. 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;312:390-409. [PubMed Abstract] -

51. Jourdain H, de Gage SB, Desplas D, Dray-Spira R. Real-world effectiveness of pre-exposure prophylaxis in men at high risk of HIV infection in France: a nested case-control study. Lancet Public Health. 2022;7:e529-e536. [PubMed Abstract] -

52. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Laboratory testing: drug-resistance testing. March 23, 2023. [HIV.gov] -

53. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. What to start: initial combination regimens for people with HIV. September 12, 2024. [HIV.gov] -

54. Liegler T, Abdel-Mohsen M, Bentley LG, et al. HIV-1 drug resistance in the iPrEx preexposure prophylaxis trial. J Infect Dis. 2014;210:1217-27. [PubMed Abstract] -

55. 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;211:1211-8. [PubMed Abstract] -

56. Mugwanya KK, Wyatt C, Celum C, et al. Changes in glomerular kidney function among HIV-1-uninfected men and women receiving emtricitabine-tenofovir disoproxil fumarate preexposure prophylaxis: a randomized clinical trial. JAMA Intern Med. 2015;175:246-54. [PubMed Abstract] -

57. Mugwanya K, Baeten J, Celum C, et al. Low risk of proximal tubular dysfunction associated with emtricitabine-tenofovir disoproxil fumarate preexposure prophylaxis in men and women. J Infect Dis. 2016;214:1050-7. [PubMed Abstract] -

58. Mugwanya KK, Wyatt C, Celum C, et al. Reversibility of glomerular renal function decline in HIV-uninfected men and women discontinuing emtricitabine-tenofovir disoproxil fumarate pre-exposure prophylaxis. J Acquir Immune Defic Syndr. 2016;71:374-80. [PubMed Abstract] -

59. Mulligan K, Glidden DV, Anderson PL, et al. Effects of Emtricitabine/Tenofovir on Bone Mineral Density in HIV-Negative Persons in a Randomized, Double-Blind, Placebo-Controlled Trial. Clin Infect Dis. 2015;61:572-80. [PubMed Abstract] -

60. Mirembe BG, Kelly CW, Mgodi N, et al. Bone Mineral Density Changes Among Young, Healthy African Women Receiving Oral Tenofovir for HIV Preexposure Prophylaxis. J Acquir Immune Defic Syndr. 2016;71:287-94. [PubMed Abstract] -

61. Liu AY, Vittinghoff E, Sellmeyer DE, et al. Bone mineral density in HIV-negative men participating in a

tenofovir pre-exposure prophylaxis randomized clinical trial in San Francisco. PLoS One. 2011;6:e23688.
[PubMed Abstract] -

62. Kasonde M, Niska RW, Rose C, et al. Bone mineral density changes among HIV-uninfected young adults in a randomised trial of pre-exposure prophylaxis with tenofovir-emtricitabine or placebo in Botswana. PLoS One. 2014;9:e90111.
[PubMed Abstract] -

63. Glidden DV, Mulligan K, McMahan V, et al. Brief Report: Recovery of Bone Mineral Density After Discontinuation of Tenofovir-Based HIV Pre-exposure Prophylaxis. J Acquir Immune Defic Syndr. 2017;76:177-182.
[PubMed Abstract] -

64. Marcus JL, Glidden DV, Mayer KH, et al. No evidence of sexual risk compensation in the iPrEx trial of daily oral HIV preexposure prophylaxis. PLoS One. 2013;8:e81997.
[PubMed Abstract] -

65. Grant RM, Anderson PL, McMahan V, et al. Lancet Infect Dis. 2014;14:820-9.
[PubMed Abstract] -

66. Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. AIDS. 2016;30:2251-2.
[PubMed Abstract] -

67. Traeger MW, Schroeder SE, Wright EJ, et al. Effects of Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection on Sexual Risk Behavior in Men Who Have Sex With Men: A Systematic Review and Meta-analysis. Clin Infect Dis. 2018;67:676-86.
[PubMed Abstract] -

68. Freeborn K, Portillo CJ. Does pre-exposure prophylaxis for HIV prevention in men who have sex with men change risk behaviour? A systematic review. J Clin Nurs. 2018;27:3254-3265.
[PubMed Abstract] -

69. Lal L, Audsley J, Murphy DA, et al. Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. AIDS. 2017;31:1709-1714.
[PubMed Abstract] -

70. Traeger MW, Cornelisse VJ, Asselin J, et al. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. JAMA. 2019;321:1380-90.
[PubMed Abstract] -

71. Traeger MW, Guy R, Asselin J, et al. Real-world trends in incidence of bacterial sexually transmissible infections among gay and bisexual men using HIV pre-exposure prophylaxis (PrEP) in Australia following nationwide PrEP implementation: an analysis of sentinel surveillance data. Lancet Infect Dis. 2022;22:1231-41.
[PubMed Abstract] -

72. Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep. 2024;73:1-8.
[PubMed Abstract] -

73. Landovitz RJ, Li S, Grinsztejn B, et al. Safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in low-risk HIV-uninfected individuals: HPTN 077, a phase 2a randomized controlled trial. PLoS Med. 2018;15:e1002690.
[PubMed Abstract] -

74. Jain S, Krakower DS, Mayer KH. The Transition From Postexposure Prophylaxis to Preexposure Prophylaxis: An Emerging Opportunity for Biobehavioral HIV Prevention. Clin Infect Dis. 2015;60 Suppl 3:S200-4.
[PubMed Abstract] -

75. Hodges-Mameletzis I, Fonner VA, Dalal S, Mugo N, Msimanga-Radebe B, Baggaley R. Pre-Exposure Prophylaxis for HIV Prevention in Women: Current Status and Future Directions. Drugs. 2019;79:1263-76.
[PubMed Abstract] -

76. Serota DP, Rosenberg ES, Sullivan PS, et al. Pre-exposure Prophylaxis Uptake and Discontinuation Among Young Black Men Who Have Sex With Men in Atlanta, Georgia: A Prospective Cohort Study. Clin Infect Dis. 2020;71:574-82.
[PubMed Abstract] -

77. Rolle CP, Onwubiko U, Jo J, Sheth AN, Kelley CF, Holland DP. PrEP Implementation and Persistence in a County Health Department Setting in Atlanta, GA. AIDS Behav. 2019;23:296-303.
[PubMed Abstract] -

78. Koren DE, Nichols JS, Simoncini GM. HIV Pre-Exposure Prophylaxis and Women: Survey of the Knowledge, Attitudes, and Beliefs in an Urban Obstetrics/Gynecology Clinic. AIDS Patient Care STDS. 2018;32:490-4.
[PubMed Abstract] -

79. Kanny D, Jeffries WL 4th, Chapin-Bardales J, et al. Racial/Ethnic Disparities in HIV Preexposure Prophylaxis Among Men Who Have Sex with Men - 23 Urban Areas, 2017. MMWR Morb Mortal Wkly Rep. 2019;68:801-6.
[PubMed Abstract] -

80. Harris NS, Johnson AS, Huang YA, et al. Vital Signs: Status of Human Immunodeficiency Virus Testing, Viral Suppression, and HIV Preexposure Prophylaxis - United States, 2013-2018. MMWR Morb Mortal Wkly Rep. 2019;68:1117-23.
[PubMed Abstract] -

81. Henny KD, Huang YA, Hoover KW. Low Human Immunodeficiency Virus (HIV) Testing Rates and No HIV Preexposure Prophylaxis Prescribed Among Female Patients Diagnosed With a Sexually Transmitted Infection, 2017-2018. Obstet Gynecol. 2020;136:1083-5.
[PubMed Abstract] -

82. Hojilla JC, Hurley LB, Marcus JL, et al. Characterization of HIV preexposure prophylaxis use behaviors and HIV incidence among US adults in an integrated health care system. JAMA Netw Open. 2021;4:e2122692.
[PubMed Abstract] -

83. Dvory-Sobol H, Shaik N, Callebaut C, Rhee MS. Lenacapavir: a first-in-class HIV-1 capsid inhibitor. Curr Opin HIV AIDS. 2022;17:15-21.
[PubMed Abstract] -

84. Cambou MC, Landovitz RJ. Challenges and Opportunities for Preexposure Prophylaxis. Top Antivir Med.

2021;29:399-406.
[PubMed Abstract] -

85. Beymer MR, Holloway IW, Pulsipher C, Landovitz RJ. Current and Future PrEP Medications and Modalities: On-demand, Injectables, and Topicals. Curr HIV/AIDS Rep. 2019;16:349-58.
[PubMed Abstract] -

86. Bekker LG, Das M, Abdool Karim Q, et al. N Engl J Med. 2024;391:1179-92.
[PubMed Abstract] -

87. Kelley CF, Acevedo-Quiñones M, Agwu AL, et al. N Engl J Med. 2024 Nov 27. Online ahead of print.
[PubMed Abstract] -

88. Chen BA, Panther L, Marzinke MA, et al. Phase 1 Safety, Pharmacokinetics, and Pharmacodynamics of Dapivirine and Maraviroc Vaginal Rings: A Double-Blind Randomized Trial. J Acquir Immune Defic Syndr. 2015;70:242-9.
[PubMed Abstract] -

89. Nel A, van Niekerk N, Kapiga S, et al. Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. N Engl J Med. 2016;375:2133-43.
[PubMed Abstract] -

References

- Andrews CD, Bernard LS, Poon AY, et al. Cabotegravir long acting injection protects macaques against intravenous challenge with SIVmac251. AIDS. 2017;31:461-467.
[PubMed Abstract] -

- Baeten JM, Palanee-Phillips T, Brown ER, et al. Use of a vaginal ring containing dapivirine for HIV-1 prevention in women. N Engl J Med. 2016;375:2121-32.
[PubMed Abstract] -

- Coelho LE, Torres TS, Veloso VG, Landovitz RJ, Grinsztejn B. Pre-exposure prophylaxis 2.0: new drugs and technologies in the pipeline. Lancet HIV. 2019;6:e788-99.
[PubMed Abstract] -

- Eppes CS, McKinney J. Incorporating Preexposure Prophylaxis Into Routine Reproductive Health Care. Obstet Gynecol. 2020;136:1080-2.
[PubMed Abstract] -

- Harawa NT, Holloway IW, Leibowitz A, et al. Serious concerns regarding a meta-analysis of preexposure prophylaxis use and STI acquisition. AIDS. 2017;31:739-40.
[PubMed Abstract] -

- Hoornenborg E, Coyer L, Achterbergh RCA, et al. Sexual behaviour and incidence of HIV and sexually transmitted infections among men who have sex with men using daily and event-driven pre-exposure prophylaxis in AMPrEP: 2 year results from a demonstration study. Lancet HIV. 2019;6:e447-e455.
[PubMed Abstract] -

- Joseph Davey DL, Pintye J, Baeten JM, et al. Emerging evidence from a systematic review of safety of pre-exposure prophylaxis for pregnant and postpartum women: where are we now and where are we heading? J Int AIDS Soc. 2020;23:e25426.
[PubMed Abstract] -

- Knox DC, Anderson PL, Harrigan PR, Tan DH. Multidrug-resistant HIV-1 infection despite preexposure prophylaxis. N Engl J Med. 2017;376:501-2.
[PubMed Abstract] -

- Liu AY, Cohen SE, Vittinghoff E, et al. Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services. JAMA Intern Med. 2016;176:75-84.
[PubMed Abstract] -

- Marshall BDL, Goedel WC, King MRF, et al. Potential effectiveness of long-acting injectable pre-exposure prophylaxis for HIV prevention in men who have sex with men: a modelling study. Lancet HIV. 2018;5:e498-e505.
[PubMed Abstract] -

- Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. Lancet HIV. 2017;4:e402-e410.
[PubMed Abstract] -

- Moodley D, Lombard C, Govender V, et al. Pregnancy and neonatal safety outcomes of timing of initiation of daily oral tenofovir disoproxil fumarate and emtricitabine pre-exposure prophylaxis for HIV prevention (CAP016): an open-label, randomised, non-inferiority trial. Lancet HIV. 2023;10:e154-e163.
[PubMed Abstract] -

- Siemieniuk RA, Sivachandran N, Murphy P, et al. Transitioning to HIV Pre-Exposure Prophylaxis (PrEP) from Non-Occupational Post-Exposure Prophylaxis (nPEP) in a Comprehensive HIV Prevention Clinic: A Prospective Cohort Study. AIDS Patient Care STDS. 2015;29:431-6.
[PubMed Abstract] -

- Trezza C, Ford SL, Gould E, et al. Lack of effect of oral cabotegravir on the pharmacokinetics of a levonorgestrel/ethinyl oestradiol-containing oral contraceptive in healthy adult women. Br J Clin Pharmacol. 2017;83:1499-1505.
[PubMed Abstract] -

- U.S. Department of Health and Humans Services (HHS). America's HIV Epidemic Analysis Dashboard (AHEAD).
[HHS] -

- Wang L, Kourtis AP, Ellington S, Legardy-Williams J, Bulterys M. Safety of tenofovir during pregnancy for the mother and fetus: a systematic review. Clin Infect Dis. 2013;57:1773-81.
[PubMed Abstract] -

- Zeggagh J, Bauer R, Delaugerre C, et al. Incidence and risk factors for recurrent sexually transmitted infections among MSM on HIV pre-exposure prophylaxis. AIDS. 2022;36:1129-34.
[PubMed Abstract] -

Figures

Figure 1 Estimated HIV Incidence in United States, 2017-2021

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.

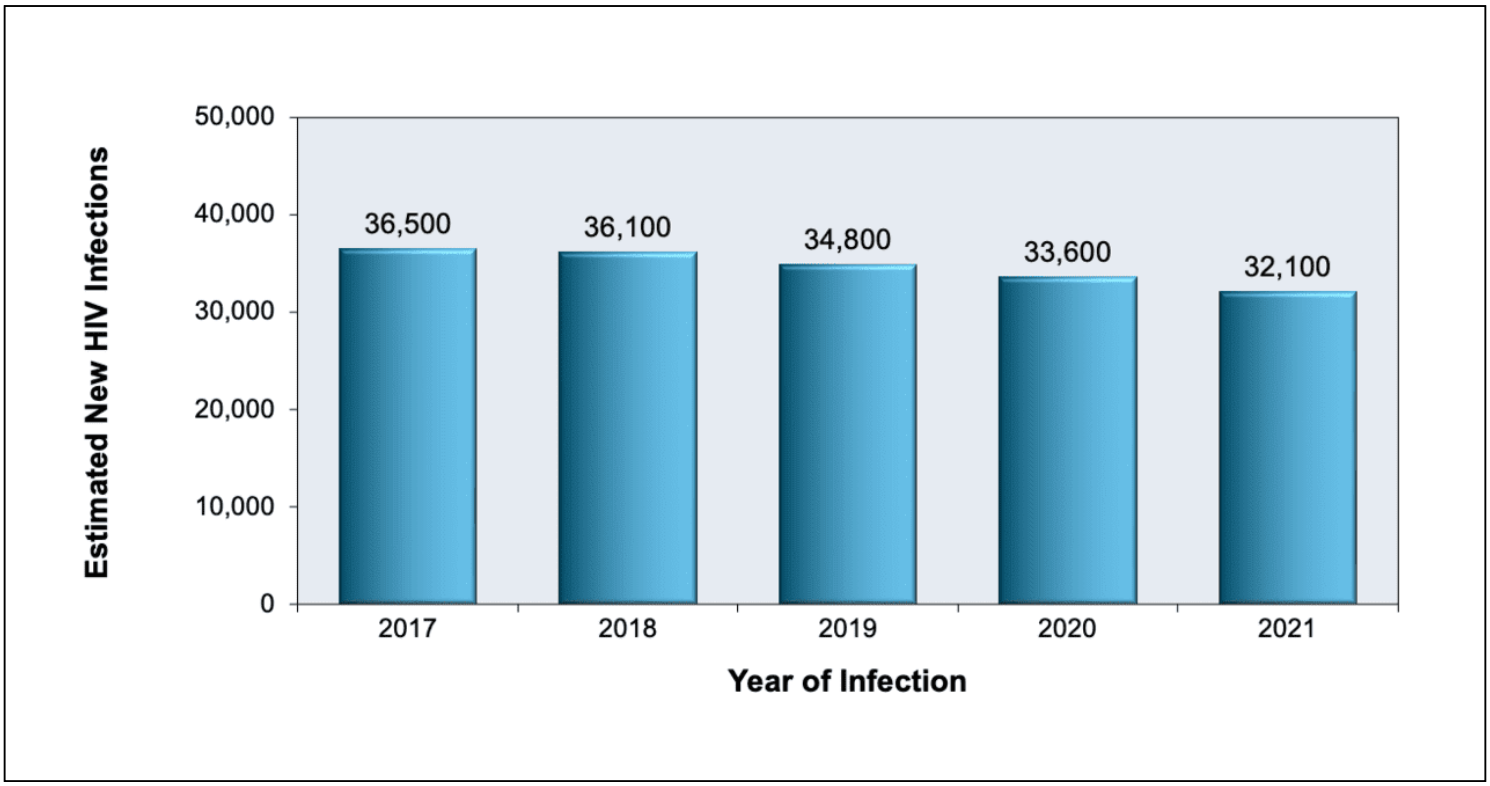

Figure 2 (Image Series) - HIV PrEP for Sexual Transmission of HIV (Image Series) - Figure 2 (Image Series) - HIV PrEP for Sexual Transmission of HIV
Image 2A: Intracellular Tenofovir and Emtricitabine

After 1-2 days of taking oral tenofovir DF-emtricitabine, the intracellular levels of tenofovir diphosphate and emtricitabine triphosphate will begin to rise. These medications must undergo phosphorylation to exert their inhibition of HIV.

Illustration by David H. Spach, MD

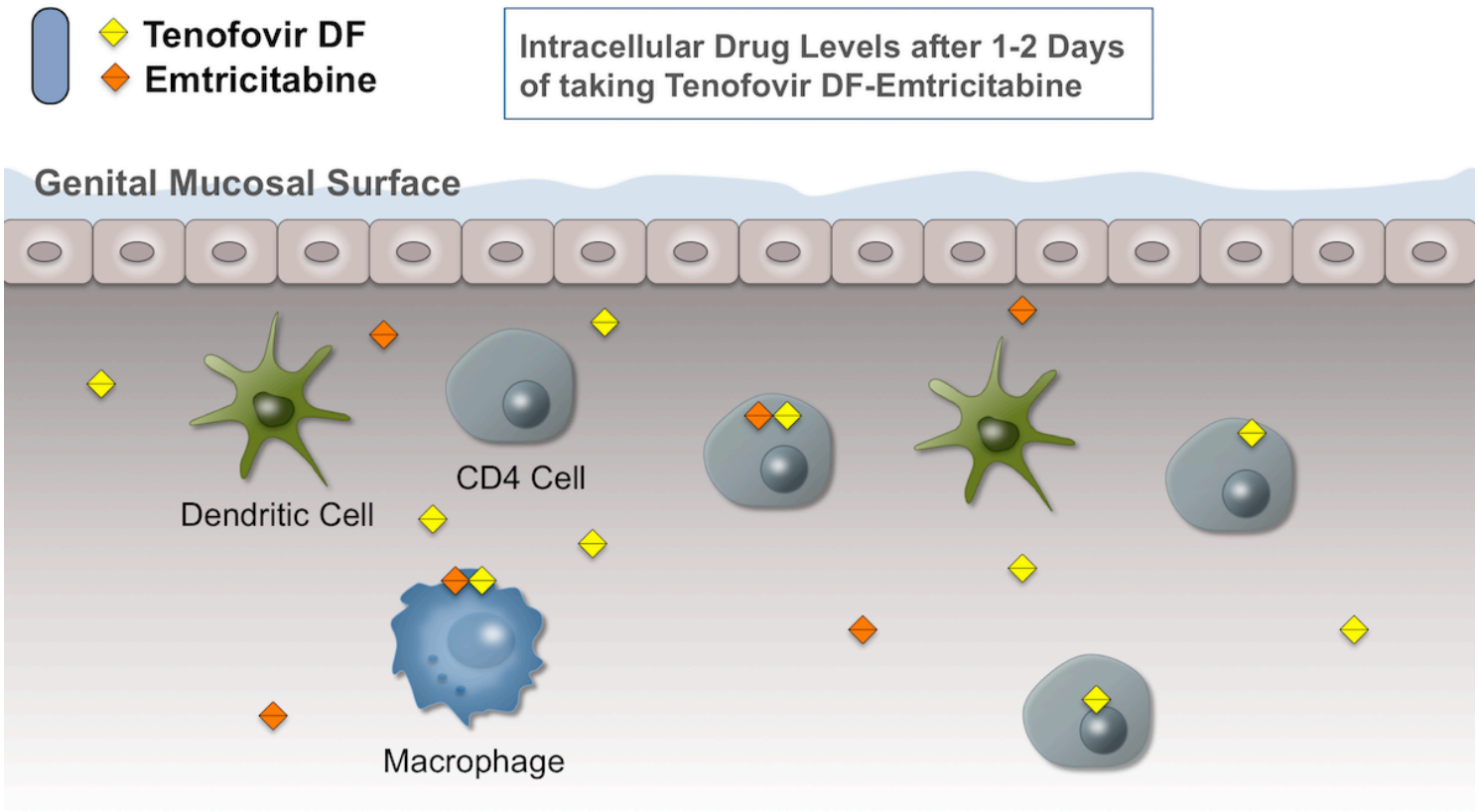

Figure 2 (Image Series) - HIV PrEP for Sexual Transmission of HIV
Image 2B: Intracellular Tenofovir and Emtricitabine

After consistently taking oral tenofovir DF-emtricitabine as HIV PrEP for 21 days, the submucosal cells susceptible to HIV infection should have high intracellular levels of tenofovir diphosphate and emtricitabine triphosphate, the active forms of these drugs.

Illustration by David H. Spach, MD

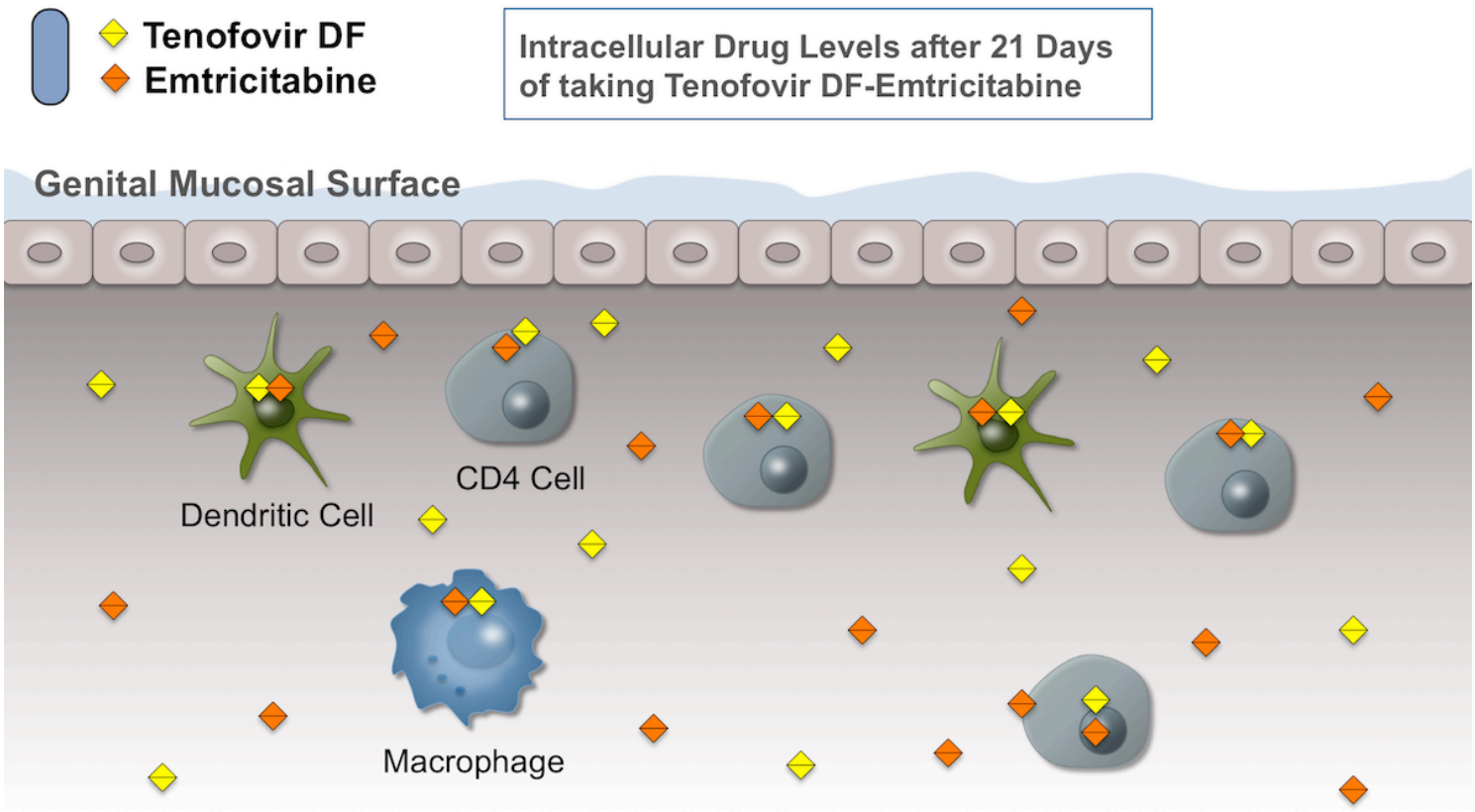

Figure 2 (Image Series) - HIV PrEP for Sexual Transmission of HIV
Image 2C: Tenofovir and Emtricitabine Blocking HIV Replication

In an individual taking PrEP who has high intracellular levels of tenofovir diphosphate and emtricitabine triphosphate, HIV infection of submucosal cells results in a dead end, since the medications block HIV reverse transcription. Thus, in this situation, HIV transmission is blocked since HIV cannot replicate and spread to other cells.

Illustration by David H. Spach, MD

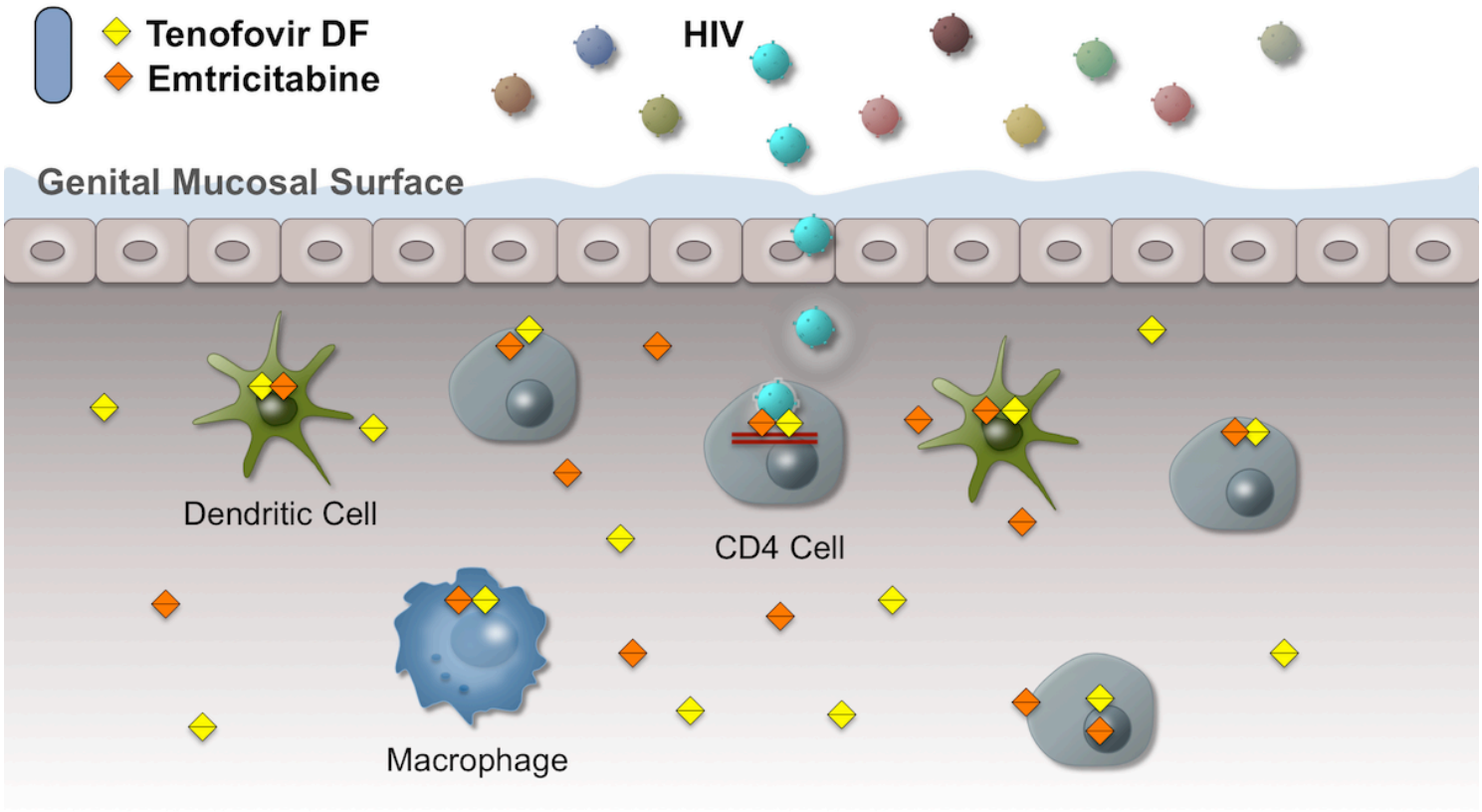

Figure 3 (Image Series) - Basic Concepts for Types of HIV PrEP (Image Series) - Figure 3 (Image Series) - Basic Concepts for Types of HIV PrEP
Image 3A: Daily Oral HIV PrEP

Illustration: David H. Spach, MD

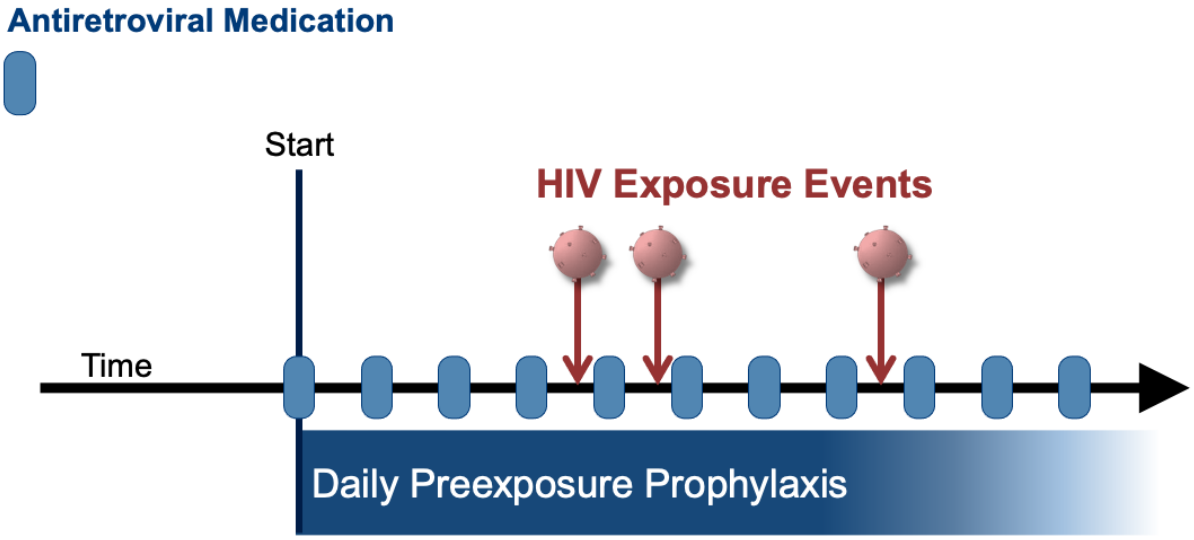

Figure 3 (Image Series) - Basic Concepts for Types of HIV PrEP
Image 3B: On-Demand (2-1-1) Oral HIV PrEP

Illustration: David H. Spach, MD

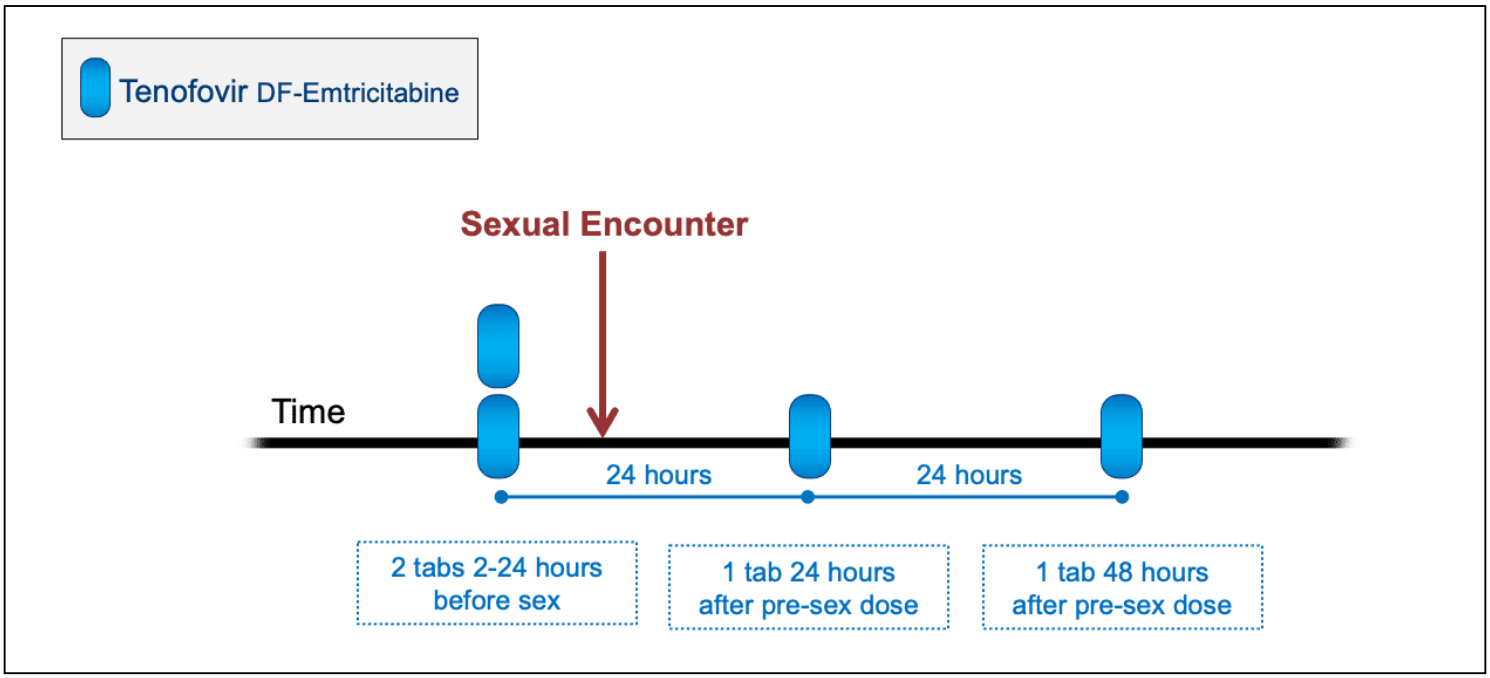

Figure 3 (Image Series) - Basic Concepts for Types of HIV PrEP
Image 3C: Long-Acting Injectable HIV PrEP

Illustration: David H. Spach, MD

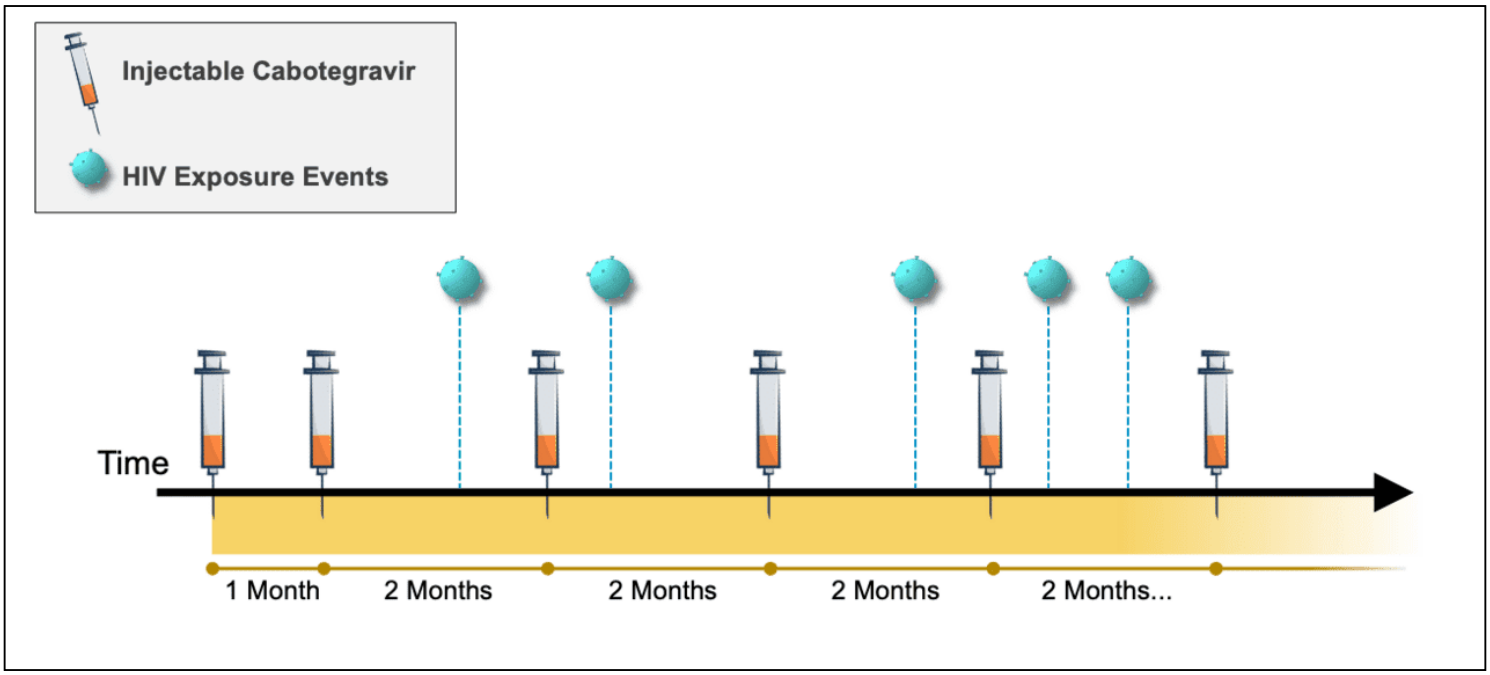

Figure 4 HIV PrEP Coverage, United States, 2017-2022

Source: (1) Centers for Disease Control and Prevention. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data United States and 6 Dependent Areas, 2021. HIV Surveillance Supplemental Report. 2023;28(No. 4):1-138. Published May 2023. (2) U.S. Health and Human Services. America's HIV Epidemic Analysis Dashboard (AHEAD). PrEP Coverage.

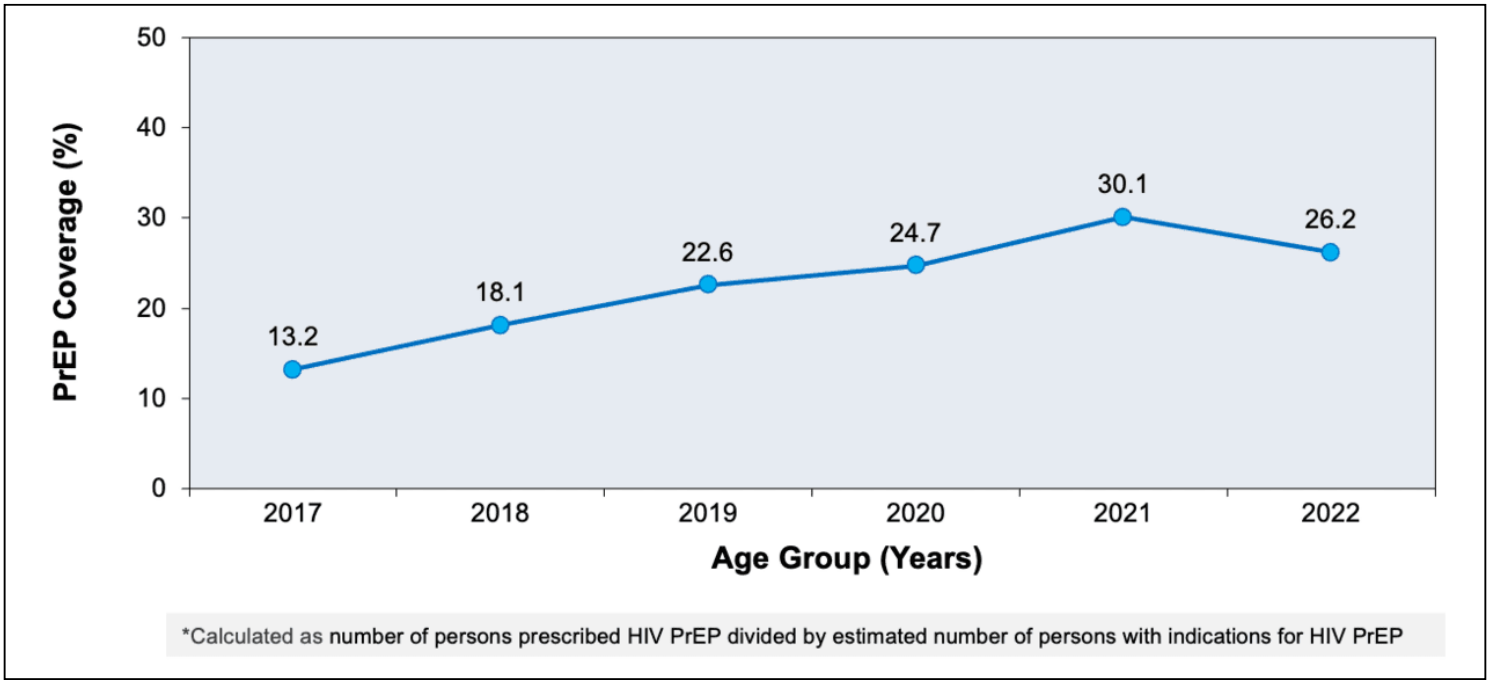

Figure 5 Estimates of PrEP Efficacy Adjusted for Adherence

In several of the key PrEP studies, efficacy is adjusted upward significantly when analyzing the data for persons with assumed adherence based on detectable antiretroviral drug levels.

Source: 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;312:390-409.

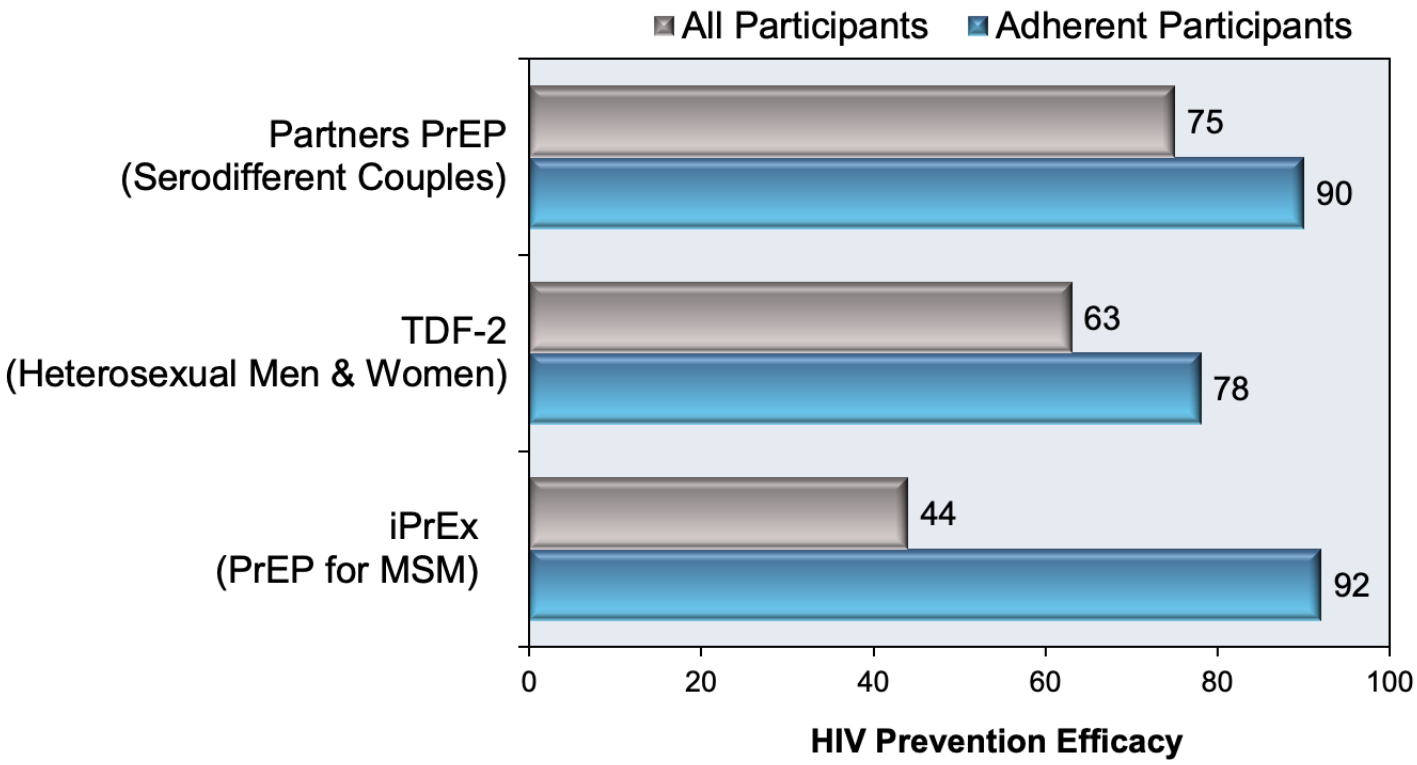

Table 1. **USPHS: Preexposure Prophylaxis for the Prevention of HIV Infection in the United States**

Key Components of Oral HIV PrEP Medication Adherence Counseling
Establish trust and bidirectional communication • Medication dosage and schedule • Management of common side effects • Relationship of adherence to the efficacy of PrEP • Signs and symptoms of acute HIV infection and recommended actions
Support adherence • Tailor daily dose to patient's daily routine • Identify reminders and devices to minimize forgetting doses • Identify and address barriers to adherence • Reinforce benefit relative to uncommon harms
Monitor behavioral adherence in a nonjudgmental manner • Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection • Reinforce success • Identify factors interfering with adherence and plan with patient to address them • Assess side effects and plan how to manage them

Source:

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108. [CDC]