

US PUBLIC HEALTH SERVICE

**PREEXPOSURE PROPHYLAXIS
FOR THE PREVENTION OF HIV
INFECTION IN THE UNITED
STATES – 2014**

CLINICAL PROVIDERS' SUPPLEMENT



Supplementary Materials:

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Introduction

Recent findings from several clinical trials have demonstrated safety¹ and a substantial reduction in the rate of HIV acquisition for men who have sex with men (MSM)^{2,3}, men and women in heterosexual discordant couples⁴, and heterosexual men and women recruited as individuals⁵ who were prescribed daily oral antiretroviral preexposure prophylaxis (PrEP) with a fixed-dose combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). The demonstrated efficacy of PrEP was in addition to the effects of repeated condom provision, sexual risk-reduction counseling, and the diagnosis and treatment of sexually transmitted infection (STI) that were provided to all trial participants. In July 2012, after reviewing these trial results, the U.S. Food and Drug Administration (FDA) approved an indication for the use of Truvada^{®1} (TDF/FTC) “in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk”^{6,7}. In July 2013, an additional clinical trial found that daily oral TDF reduced the rate of HIV acquisition for injection drug users (IDU) (also called persons who injection drugs [PWID])⁸.

On the basis of these trial results and the FDA approval, the U.S. Public Health Service has published a comprehensive clinical practice guideline for the use of PrEP for the prevention of HIV infection in the United States <http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>.

This supplement to the PHS PrEP Clinical Practice Guidelines is intended to provide additional information that may be useful to clinicians providing PrEP. As additional materials become available, this document will be updated.

- Section 1 Contains a template checklist that clinicians can complete and share with patients to document the services provided to PrEP patients and the actions expected from patients to maximize the efficacy and safety of PrEP.
- Sections 2-4 Contain templates for informational handouts that can be provided to patients
- Section 5 Contains the HIV incidence Risk Index for MSM, a tool that clinicians may use to quickly and systematically determine which men are at especially high risk for acquiring HIV infection, for whom PrEP may be indicated.
- Sections 6-7 Contain more detailed information than that included in the guidelines about methods and resources for counseling patients receiving PrEP about medication adherence and HIV risk reduction behaviors.
- Sections 8-9 Contain information relevant to administrative and billing codes for PrEP related services
- Section 10 Documents the methods used to develop the PHS PrEP Clinical Practice Guidelines

¹ Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

Section 1 Patient/Provider Checklist

Organization/Clinic Name

CHECKLIST FOR INITIATING PREEXPOSURE PROPHYLAXIS (PrEP)

Print name of provider

Print name of patient

Today's date (month/day/year)

Provider Section

I have provided this patient with the following: (check all as completed):

- Assessment for possible acute HIV infection
- Indicated laboratory screening to determine indications for these medications
- An HIV risk assessment to determine whether PrEP is indicated for this patient
- A medication fact sheet listing dosing instructions and side effects
- Counseling or a referral for counseling on condom use and any other HIV risk-reduction methods this patient may need
- Advice on methods to help the patient to take medication daily as prescribed
- Information about PrEP use during conception and pregnancy (when indicated)
- A prescription for Truvada (300 mg tenofovir disoproxil fumarate, 200 mg emtricitabine)
- A follow-up appointment date

As the provider, I will:

- Limit refill periods to recommended intervals for repeat HIV testing (at least every 3 months)
- Conduct follow-up visits at least every 3 months that include the following:
 - Assessment of HIV status (including signs or symptoms of acute HIV infection)
 - Assessment of side effects and advice on how to manage them
 - Assessment of medication adherence and counseling to support adherence
 - Assessment of STI symptoms, HIV risk behavior and counseling support for risk-reduction practices
- Inform the patient of any new information about PrEP and respond to questions

Patient Section

It has been explained to me that:

- Taking a dose of PrEP medication every day may lower my risk of getting HIV infection
- This medicine does not completely eliminate my risk of getting HIV infection, so I need to use condoms during sex
- This medicine may cause side effects so I should contact my provider for advice by calling _____ if I have any health problems
- It is important for my health to find out quickly if I get HIV infection while I'm taking this medication, so
 - I will contact my provider right away if I have symptoms of possible HIV infection (fever with sore throat, rash, headache, or swollen glands)
- My provider will test for HIV infection at least once every 3 months

Therefore, I will:

- Try my best to take the medication my provider has prescribed every day
- Talk to my provider about any problems I have in taking the medication every day
- Not share the medication with any other person
- Attend all my scheduled appointments
- Call _____ to reschedule any appointments I cannot attend

Give one copy to patient

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

Frequently Asked Questions

What is PrEP?

“PrEP” stands for **pre**exposure **pro**phylaxis. The word “prophylaxis” (pronounced pro fil ak sis) means to prevent or control the spread of an infection or disease. The goal of PrEP is to prevent HIV infection from taking hold if you are exposed to the virus. This is done by taking a pill that contains 2 HIV medications every day. These are the same medicines used to stop the virus from growing in people who are already infected.

Why take PrEP?

The HIV epidemic in the United States is growing. About 50,000 people get infected with HIV each year. More of these infections are happening in some groups of people and some areas of the country than in others.

Is PrEP a vaccine?

No. PrEP medication does not work the same way as a vaccine. When you take a vaccine, it trains the body’s immune system to fight off infection for years. You will need to take a pill every day by mouth for PrEP medications to protect you from infection. PrEP does not work after you stop taking it. The medication that was shown to be safe and to help block HIV infection is called “Truvada” (pronounced tru va duh). Truvada is a combination of 2 drugs (tenofovir and emtricitabine). These medicines work by blocking important pathways that the HIV virus uses to set up an infection. If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can often stop the HIV virus from establishing itself and spreading in your body. If you do not take the Truvada pills every day, there may not be enough medicine in your blood stream to block the virus.

Should I consider taking PrEP?

PrEP is not for everyone. Doctors prescribe PrEP for some patients who have a very high risk of coming in contact with HIV by not using a condom when they have sex with a person who has HIV infection. You should consider PrEP if you are a man or woman who sometimes has sex without using a condom, especially if you have a sex partner who you know has HIV infection. You should also consider PrEP if you don’t know whether your partner has HIV infection but you know that your partner is at risk (for example, your partner inject drugs or is having sex with other people in addition to you) or if you have recently been told by a health care provider that you had a sexually transmitted infection. If your partner has HIV infection, PrEP may be an option to help protect you from getting HIV infection while you try to get pregnant, during pregnancy, or while breastfeeding.

How well does PrEP work?

PrEP was tested in several large studies with men who have sex with men, men who have sex with women, and women who have sex with men. All people in these studies (1) were tested at the beginning of the trial to be sure that they did not have HIV infection, (2) agreed to take an oral PrEP tablet daily,

(3) received intensive counseling on safer-sex behavior, (4) were tested regularly for sexually transmitted infections, and (5) were given a regular supply of condoms.

Several studies showed that PrEP reduced the risk of getting HIV infection.

- Men who have sex with men who were given PrEP medication to take, were 44% less likely to get HIV infection than were those men who took a pill without any PrEP medicine in it (a placebo). Forty-four percent was an average that included men who didn't take the medicine every day and those who did. Among the men who said they took most of their daily doses, PrEP reduced the risk of HIV infection by 73% or more, up to 92% for some.
- Among men and women in couples in which one partner had HIV infection and the other partner initially did not ("HIV-discordant" couples), those who received PrEP medication were 75% less likely to become infected than those who took a pill without any medicine in it (a placebo). Among those who said they took most of their daily doses, PrEP reduced the risk of HIV infection by up to 90%.
- In one study of men and women who entered the study as individuals (not as a couple), PrEP worked for both men and women in one study: those who received the medication were 62% less likely to get HIV infection; those who said they took most of their daily doses, were 85% less likely to get HIV infection. But in another study, only about 1 in 4 women (<26%) had PrEP medication found in their blood when it was checked. This indicated that few women were actually taking their medication and that study found no protection against HIV infection.

More information on the details of these studies can be found at <http://www.cdc.gov/hiv/prep>.

Is PrEP safe?

The clinical trials also provided safety information on PrEP. Some people in the trials had early side effects such as an upset stomach or loss of appetite but these were mild and usually went away within the first month. Some people also had a mild headache. No serious side effects were observed. You should tell your doctor if these or other symptoms become severe or do not go away.

How can I start PrEP?

If you think you may be at high risk for HIV, talk to your doctor about PrEP. If you and your doctor agree that PrEP might reduce your risk of getting HIV infection, you will need to come in for a general health physical, blood tests for HIV, and tests for other infections that you can get from sex partners. Your blood will also be tested to see if your kidneys and liver are functioning well. If these tests show that PrEP medicines are likely to be safe for you to take and that you might benefit from PrEP, your doctor may give you a prescription after discussing it with you.

Taking PrEP medicines will require you to follow-up regularly with your doctor. You will receive counseling on sexual behaviors and blood tests for HIV infection and to see if your body is reacting well to Truvada. You should take your medicine every day as prescribed, and your doctor will advise you about ways to help you take it regularly so that it stands the best chance to help you avoid HIV infection. Tell your doctor if you are having trouble remembering to take your medicine or if you want to stop PrEP.

If I take PrEP can I stop using condoms when I have sex?

You should not stop using condoms because you are taking PrEP. If PrEP is taken daily, it offers a lot of protection against HIV infection, but not 100%. Condoms also offer a lot of protection against HIV infection if they are used correctly every time you have sex, but not 100%. PrEP medications don't give you any protection from other infections you can get during sex, but condoms do. So you will get the most protection from HIV and other sexual infections if you consistently take PrEP medication and consistently use condoms during sex.

How long do I need to take PrEP?

You should discuss this with your doctor. There are several reasons that people stop taking PrEP. If your risk of getting HIV infections becomes low because of changes that occur in your life, you may want to stop taking PrEP. If you find you don't want to take a pill every day or often forget to take your pills, other ways of protecting yourself from HIV infection may work better for you. If you have side effects from the medication that are interfering with your life or if blood tests show that your body is reacting to PrEP in unsafe ways, your doctor may stop prescribing PrEP for you.

Section 3 Truvada Medication Information Sheet

Truvada Medication Information Sheet for Patients

Brand name: Truvada (tru va duh)

Generic name: tenofovir disoproxil fumarate and emtricitabine

Why is this medication prescribed?

- Truvada is one of several medications that are currently used to treat human immunodeficiency virus (HIV) and hepatitis B virus infection.
- Truvada is now being used to *prevent* HIV infection.
- Truvada is sometimes prescribed to some people who do not have HIV infection (for example, those who do not always use condoms or who have a sex partner that has HIV infection) to help reduce their chances of getting HIV infection
- When you take Truvada to prevent HIV infection, doctors refer to this use as “pre-exposure prophylaxis” or “PrEP”.

How does Truvada (PrEP) help prevent HIV infection?

- HIV is a virus that attacks your body’s immune cells (the cells that work to fight infections).
- The 2 medications that make up Truvada (tenofovir and emtricitabine) block important pathways that viruses use to set up infection.
- If you take Truvada as PrEP daily, the presence of the medication in your bloodstream can sometimes stop the virus from establishing itself and slow the spread of HIV in your body.
- By itself, PrEP with Truvada does not work all the time so you should also use condoms during sex for the most protection from HIV infection.

How should this medicine be used?

- You must take one tablet of Truvada by mouth every day .
- Follow the directions on your prescription label carefully, and ask your doctor or pharmacist to explain any part you do not understand.
- Do not stop taking Truvada without talking to your doctor. When your supply of Truvada starts to run low, contact your doctor or pharmacist to get more.
- You may be at higher risk of becoming infected with HIV if you miss doses or stop taking Truvada than if you take it every day.

What special precautions should I follow?

Before taking Truvada (tenofovir and emtricitabine) you must do the following:

- Tell your doctor and pharmacist if you are allergic to tenofovir, emtricitabine, or any other medications.
- Tell your doctor and pharmacist about all prescription and nonprescription medications, (vitamins, nutritional supplements, and herbal products) you are taking. Your doctor may need to change the doses of your medications or monitor you carefully for side effects.
- Tell your doctor if you have or have ever had kidney or liver disease.
- Tell your doctor if you become pregnant or if you are breastfeeding

What special dietary instructions should I follow?

- Continue your normal diet unless your doctor tells you otherwise.

What should I do if I forget a dose?

- Take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule.
- Do not take a double dose to make up for a missed one.

What side effects can this medication cause?

You may experience the following side effects while taking Truvada:

- upset stomach
- headache
- vomiting
- loss of appetite

These side effects usually fade during the first month of taking Truvada for PrEP. Tell your doctor if any of these symptoms are severe or do not go away.

Truvada may cause other side effects. Some side effects can be serious. Call your doctor immediately if you have any unusual problems while taking this medication or if you have any of the following:

- fever or chills especially with
- sore throat, cough, rash or other signs of infection

If you experience a serious side effect, you or your doctor may send a report to the Food and Drug Administration's (FDA) MedWatch Adverse Event Reporting program online (at <http://www.fda.gov/Safety/MedWatch>) or by phone (1-800-332-1088).

How should I store Truvada in my home?

- You should keep Truvada in the container it came in, tightly closed, and out of reach of children.
- You must store it at room temperature and away from excessive heat and moisture.
- Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

What should I do in case of emergency/overdose?

- In case of overdose, call your local poison control center at 1-800-222-1222. If the person has collapsed or is not breathing, call local emergency services at 911.

What other information should I know?

- Do not let anyone else take your medication.
- Ask your pharmacist if you have any questions about refilling your prescription.
- Write a list of all of your prescription and over-the-counter medicines, as well as any vitamins, minerals, or other dietary supplements that you take.
- Bring your medication list with you each time you visit a doctor or if you are admitted to a hospital. Keep it with you always in case of emergencies.

Section 4 Patient Information Sheet – Acute HIV Infection

Information about Acute HIV Infection and PrEP

What is acute HIV Infection?

HIV stands for human immunodeficiency virus. This is the virus that causes AIDS.

Acute HIV infection is a name for the earliest stage of HIV infection, when you first get infected with the HIV virus. It is sometimes also called primary HIV infection. Many people with acute HIV infection have the following:

- A fever
- A tired feeling
- Swollen lymph nodes (also called lymph glands)
- Swollen tonsils (also called tonsillitis)
- A sore throat
- Joint and muscle aches
- Diarrhea
- A rash

These signs and symptoms of acute HIV infection can begin a few days after you are exposed to HIV and usually last for about 14 days. They could last for just a few days, or they could last for several months.

You might not realize your illness is acute HIV infection. For one thing, you may not have known that the person you had sex with had HIV infection. And the signs and symptoms of HIV infection may feel just like other common virus infections like flu, a cold, sore throat, or mononucleosis (mono).

What tests can show that I have acute HIV infection?

When HIV enters your body, it moves inside white blood cells called CD4 lymphocytes. HIV takes over the CD4 cells and makes billions of copies of the virus each day. The virus spread through your body.

Your body tries to defend itself against HIV by making antibodies (these antibodies try to block the virus from spreading in your body). Most HIV tests check to see if antibodies against HIV are in your blood. But it takes a few weeks before your body makes enough antibodies for the usual HIV tests to see them.

However, when you have acute HIV infection, you have a high amount of the HIV virus in your blood. Special tests can measure the amount of HIV in your blood. At the time you have acute HIV infection, you probably won't have enough HIV antibodies in your blood to measure, but you will have enough virus to measure. So if the blood tests do not find any antibody but do see the virus, your doctor will know that you're feeling sick because you have acute HIV infection.

How does it help to find out I have HIV at an early stage?

First, PrEP is used to help lower your chances of getting HIV infection. If you already have acute HIV infection you should not take PrEP.

Second, while PrEP helps protect people, especially when they take their doses every day, it is still possible to get HIV infection. So if you are taking PrEP and have the signs and symptoms mentioned above, it is important to see your doctor to be checked. If you have some other infection, like the flu, you should continue your PrEP medicines but if it is discovered that you have acute HIV infection, you should stop taking PrEP as soon as your tests show that you have HIV infection

Third, people who take PrEP for more than a couple of weeks while they have HIV infection can easily develop virus that can't be treated with those same drugs (resistant virus). So finding out quickly that you have HIV infection and stopping PrEP can protect your long term health and keep your treatment options open.

And fourth, when people have lots of virus in their body during acute HIV infection, they are more likely to pass the virus on to people they have sex with, especially since they may not know yet that they have gotten infected. For example, if your last HIV test result was negative and your partner also had a recent negative HIV test result, you might choose to have sex without a condom just at the time when it's very likely you would pass the virus on. So the sooner you know you have become infected, the more careful you can be to protect others from getting HIV infection.

How is HIV treated?

People who have HIV infection are treated with combinations of 3 or more medicines that fight HIV. Some doctors start people on treatment medications as soon as they become infected; other doctors wait for a while because the greatest benefits to a person's health are seen after they have been infected a while. Early treatment also reduces the chances that a person with HIV infection will pass the virus on to their sex partners.

What do I do if I suspect I might have acute HIV infection?

First, contact your doctor's office and arrange to be examined and have the right blood tests.

Second, discuss with your doctor whether to stop your PrEP medications or continue them until your test results are back.

Third, be especially careful to use condoms and take other safer sex measures to protect your partner(s).

Section 5 Provider Information Sheet – PrEP during Conception, Pregnancy, and Breastfeeding

Information for Clinicians

Counseling Patients about PrEP Use During Conception, Pregnancy, and Breastfeeding

PrEP use may be one of several options to help protect the HIV-negative male or female partner in a heterosexual HIV-discordant couple during attempts to conceive^{1,2}.

DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission

Panel's Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples

For Couples who Want to Conceive

For Both Concordant (Both Partners are HIV-Infected)/Discordant Couples:

- Expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple (**AIII**).
- Partners should be screened and treated for genital tract infections before attempting to conceive (**AII**).
- The HIV-infected partner should attain maximum viral suppression before attempting conception (**AIII**).

For Discordant Couples:

- Combination antiretroviral therapy (cART) for the infected partner may not be fully protective against sexual transmission of HIV.
- Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission (**CIII**). The utility of PrEP of the uninfected partner when the infected partner is receiving cART has not been studied.

Discordant Couples with HIV-Infected Female:

- The safest conception option is artificial insemination, including the option of self-insemination with a partner's sperm during the peri-ovulatory period (**AIII**).

Discordant Couples with HIV-Infected Male:

- The use of donor sperm from an HIV-uninfected male with artificial insemination is the safest option.
- When the use of donor sperm is unacceptable, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered (**AII**).
- Semen analysis is recommended for HIV-infected males before conception is attempted to prevent unnecessary exposure to infectious genital fluid when the likelihood of getting pregnant is low because of semen abnormalities (**AIII**).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

The following information is provided to help you inform your patients of current information about potential risks and benefits of PrEP use so that you and your patients can make an informed decision.

Key Points

- Provide education about PrEP and other methods of conception that minimize the risk of HIV transmission to both members of an HIV-discordant couple whenever possible.
- During counseling, include discussion of what is currently known and unknown about
 - Potential benefits
 - Potential risks
- If you prescribe PrEP, include the following in counseling:
 - Importance of adherence to daily doses of medication
 - Importance of continuing condom use after conception to protect against sexually transmitted infections and to add protection against HIV infection
 - Signs and symptoms of acute HIV infection and the need for urgent HIV testing if HIV infection is suspected

FOR AN HIV-NEGATIVE MAN PLANNING PREGNANCY WITH AN HIV-POSITIVE FEMALE PARTNER

Options

Reducing the risk of HIV acquisition by an HIV-negative man during conception can be achieved by use of the following, singly or ideally in combination^{3,4}:

- Antiretroviral treatment of the HIV-positive female partner to achieve an undetectable viral load⁵
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt
- Intravaginal insemination⁶ (either at home or in the clinic) with a fresh semen sample

OR

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation.

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%-75%. Higher levels of protection ($\geq 90\%$) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication^{7,8}.

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1-4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

FOR AN HIV-NEGATIVE WOMAN PLANNING PREGNANCY WITH AN HIV-POSITIVE MALE PARTNER

Options

Reducing the risk of HIV acquisition by an HIV-negative woman during conception can be achieved by use of the following, singly or ideally in combination^{3,4}:

- Antiretroviral treatment of the HIV-positive male partner to achieve an undetectable viral load⁵
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt
- Intravaginal⁶ or intrauterine insemination, or intracytoplasmic sperm injection with a semen sample processed by “sperm washing” and confirmed to have a negative test result for the presence of remnant HIV⁹

OR

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation in the female partner¹⁰.

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%-75%. Higher levels of protection ($\geq 90\%$) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication^{7,8}.

The risk of HIV acquisition increases during pregnancy¹¹, as does the risk of HIV transmission to an infant born to a mother who becomes infected during pregnancy or breastfeeding¹². Therefore, an HIV-negative woman whose sexual partner/spouse has HIV infection may benefit from continuing PrEP use throughout her pregnancy and breastfeeding to protect herself and her infant.

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1-4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

In PrEP trials women were taken off medication as soon as pregnancy was detected. During these trials, no health problems have been associated with PrEP use by women in early pregnancy or for their offspring. However, the long-term safety of PrEP taken HIV-uninfected women after fetal (during pregnancy) or infant (during breastfeeding) exposure is not yet determined.

No adverse effects have been found among infants exposed to TDF/FTC when the medications were taken as part of a treatment regimen for HIV-infected women during pregnancy¹³⁻¹⁵ or during breastfeeding (for which data suggest limited drug exposure^{16,17}).

If you prescribe PrEP to a woman while pregnant, you are encouraged to prospectively and anonymously submit information about the pregnancy to the Antiretroviral Use in Pregnancy Registry (<http://www.apregistry.com/>).

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Section 6 MSM Risk Index

Epidemiologic studies have identified a wide range of personal, relationship, partner, social, cultural, network, and community factors that may be associated with the presence of HIV infection. However, to provide PrEP (or other intensive HIV prevention services), it is necessary to briefly and systematically screen for key information about those factors that are predictive of very high risk of acquiring HIV infection.

This section contains a tool that clinicians may use to quickly and systematically determine which MSM are at especially high risk of acquiring HIV infection, and for whom PrEP may be indicated.

Screening tools are not yet available for other populations that may use PrEP (e.g., heterosexual women and men, IDU). As other screening tools are identified or developed, they will be added in updates to this supplement.

MSM Risk Index²⁵

1	How old are you today?	If <18 years, score 0 If 18-28 years, score 8 If 29-40 years, score 5 If 41-48 years, score 2 If 49 years or more, score 0	_____
2	In the last 6 months, how many men have you had sex with?	If >10 male partners, score 7 If 6-10 male partners, score 4 If 0-5 male partners, score 0	_____
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom?	If 1 or more times, score 10 If 0 times, score 0	_____
4	In the last 6 months, how many of your male sex partners were HIV-positive?	If >1 positive partner, score 8 If 1 positive partner, score 4 If <1 positive partner, score 0	_____
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) without a condom with a man who was HIV-positive?	If 5 or more times, score 6 If 0 times, score 0	_____
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	If yes, score 6 If no, score 0	_____

			TOTAL SCORE*

Add down entries in right column
to calculate total score

* If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.
If score is below 10, provide indicated standard HIV prevention services.

Section 7 Supplemental Counseling Information – Medication Adherence

MEDICATION EDUCATION AND ADHERENCE SUPPORT

Understanding what patients know about PrEP and why they are considering taking it can reveal important information about potential adherence facilitators or barriers. You may wish to begin discussion through a conversation (e.g., “Let’s talk. Tell me what you know about PrEP” or “Why do you want to take PrEP?”) that can help clarify whether the patient understands the risks and benefits of PrEP given their current sexual behavior and protection strategies, and how their reason(s) for taking PrEP may affect medication adherence.

Adherence to prophylactic regimens is strongly associated with patient understanding of drug information. Patients beginning a PrEP regimen need a very clear understanding of how to take their medications (i.e., when it is to be administered, how many pills to take at each dose) and what to do if they experience problems (e.g., how long outside the dosing window is a dose considered “missed”, what to do if they miss a dose). Side effects are often a cause of non-adherence, so a plan for addressing them should be made. It is recommended that you and the patient develop a plan for addressing side effects that the patient would consider intolerable. The plan may include over-the-counter medications that can mitigate symptoms and should stress the need to use condoms consistently if the patient stops taking PrEP medication.

You should also discuss the need for the patient to be tested for HIV every 3 months. Although patients may feel anxious about such frequent testing, it is important that patients understand that frequent testing is needed to prevent drug resistance if they become infected while taking PrEP medication. Be prepared to answer other questions, such as: “What if people see the medications and think I am HIV-positive?” “Do I need to tell my partner?” “Do I need to take the medication regularly when I am not having sex?”; “Will it help to take extra doses?” “How long can I take the medication?”. When you begin a discussion around adherence, emphasize the normalcy of missing occasional doses and the importance of a plan to try to minimize missed doses (see Box 6.1 for an example of how to introduce this issue).

Box 6.1: Adherence Discussion

You are going to have to take the pill once a day, every day. Although this seems easy, we know that people forget to take their medicines, especially when they are not sick. It will be easier to take your medicine if you think through now some plans about how you’ll do it. First, let’s briefly discuss your experiences other times you might have taken medicine.

- *When you’ve taken medicines before, how did you remember to take them?
- Please tell me about any problems you had taking your pill.
- *What was most helpful for remembering to take them?

An adherence plan should include the following: (1) tailoring the dosing time to correspond with the patient's regularly scheduled activities so that medication taking becomes integrated into the patient's daily routine, (2) using reminders or technical devices (e.g., beepers, alarms) to minimize forgetfulness, (3) considering organizational needs and tools (e.g., calendars, strategies for weekends away from home) to address changes in routine and schedule, and (4) reviewing disclosure issues to identify those who can support the patient's intentions to adhere or barriers to adherence due to lack of disclosure/privacy at home. (See Box 6.2 for sample questions.)

Box 6.2: Developing an adherence plan

OK, now let's come up with a plan for taking your medicine.

1. Scheduling

What is your schedule like during a typical week day?

At what point in the day do you think it would be easiest to take the pill? That is, is there a time when you are almost always at home, and not in too much of a rush?

How does your schedule differ on weekends?

2. Reminder devices

How will you remember to take the pill each day?

One way to remember is to take the pill at the same time that you are doing another daily task, such as brushing your teeth or eating breakfast. Which of your daily tasks might be used for this purpose? Try to pick something that happens every day. Sometimes we might pick something that is not always done on the weekends or during other days, and then we are more likely to forget. (For example, **One potential example follows:** sometimes I don't shave on Saturdays, but I always brush my teeth, so linking taking the medicine to brushing my teeth might be better than linking it to shaving.) It also helps to store the pills near the place where you perform this daily task.

Some people use a reminder device to help them remember. Do you have any reminder devices that you have used in the past? For example, watches, beepers, or cell phones.

3. Organizational skills

Where will you store the bottle of pills?

When you travel or spend the night outside of your home, what will you do about taking the pill?

4. Social support & disclosure

Who in your household will know the reason that you are taking the pills? Are they supportive of you taking them? Are there individuals who might make assumptions about your serostatus because you have these medicines?

You may wish to explore other potential barriers that emerged in initial conversations (e.g., beliefs and attitudes), including factors (e.g., as substance use, depression or unstable housing) known to negatively affect medication adherence, such. To adhere to PrEP medication well, some patients may need access to mental health or social services.

MONITORING PREP PATIENTS: ASSESSING SIDE EFFECTS AND ADHERENCE

Assess medication adherence as well as adherence to HIV testing at every visit. Self-reported adherence is typically an overestimate of true adherence, but patients may overreport their adherence when they fear that a more accurate report would result in a negative judgment from their clinician. When asking patients about their adherence, do your best to adopt a non-judgmental attitude, giving the patient permission to share adherence difficulties without worrying that you will reproach them. Asking patients to help you understand how they are doing with their medications will provide more information and thus allow for a better diagnostic picture of a patient's needs than will a more prescriptive approach.

Begin follow-up visits by asking the patient how well they have been doing with taking all of their medicines as scheduled. Accept more general responses (e.g., “so so”, “pretty good”, “excellent”, “perfect”) before asking for specific information about the frequency and the context of missed doses. Provide reinforcement for patients who report that they are doing well: ask questions such as “What are you doing to keep this going so well?” or “That’s great. Can you see anything getting in the way of this?” These exchanges can help solidify the factors that are supporting your patients’ adherence while helping them prepare for any barriers that may arise in the future.

When talking with patients who are not reporting perfect adherence, ask as to how many doses they have missed during a specific period. Assessing a longer period (e.g., 30 days, 7 days) is preferred to shorter periods (e.g., 3 days), not only because adherence can vary with changes in schedule (e.g., weekends, holidays) that may not have occurred during the shorter assessment period, but because many patients increase medication-taking just before medical appointments, a phenomenon supported by blood level assessments in the iPrEx trial.² When asking about many doses were missed (e.g., “In the last 30 days, how many times have you missed your PrEP medication?”), also (1) ask whether this was typical since their last clinic visit in order to gain a sense of adherence patterns, (2) ask for specific information about when they most recently missed dose(s), and (4) determine the circumstances during which those missed doses occurred (e.g., “Where were you?” “Who were you with?” “What happened just before you were supposed to take your medicine?”). Asking what happened on the day the dose was missed, and getting the patient’s perspective on what generally gets in the way of taking medications regularly, will facilitate a conversation that will help to identify the patient’s specific adherence barriers as well as the type of adherence support the patient needs.

On the basis of this conversation, develop a plan to address adherence barriers. Questions such as “What do you think you can do differently?” “What things make it easier to take your medications?” “What things need to happen for you to take your medications regularly?” or “What might you try [to not forget your weekend doses]?” bring the patient into the planning process and thus facilitate identification of the strategies most likely to be implemented. It’s important for you to be familiar with a range of adherence strategies that can be shared with patients who require help with this task.

Finally, assess whether the patient is experiencing any side effects of medication, the severity of the side effects, and their role as an adherence barrier determined. Currently, most of what is

known about antiretroviral therapy (ART) side effects is derived from patients with HIV. Healthy people may be more concerned about side effects than HIV patients. Try to determine whether clinical symptoms attributed to PrEP medication could possibly be due to other disorders (e.g., depression) or natural processes (e.g., aging). If necessary, include medications to treat side effects in the adherence plan.

Section 8 Supplemental Counseling Information – HIV Risk Reduction

Determining whether the patient is a good candidate for PrEP is not strictly objective, and should be based on an ongoing discussion between you and your patient. Risk screening can be conducted using various approaches: face-to-face interviews, written forms, or computer-based tools. Written forms and computer-based tools are effective and can be conducted with fewer staff resources²⁶. However, self-administered written forms are not recommended for persons with low literacy.

Using risk screening information and the HIV test results, provide your patients with services that are appropriate for their level of risk and are tailored to their prevention needs. Patients who report no or few risk factors, may have minimal prevention needs. In the absence of other information, these patients do not need PrEP. For patients for whom PrEP is appropriate, provide risk-reduction counseling and support services before, during, and after PrEP you prescribe PrEP.

SEXUAL RISK REDUCTION COUNSELING

Address the sexual health of your patients, including risk behaviors that increase the likelihood of acquiring HIV or other sexually transmitted infections. Several discussion areas are recommended even in brief discussions of sexual risk behavior. For patients who demonstrate an elevated risk of sexual HIV acquisition, provide a brief risk reduction intervention onsite or link them to a program that provides those services (see <http://www.effectiveinterventions.org>). For patients who are continuing to engage in high-risk sexual behaviors or who need additional prevention services (beyond a brief risk-reduction intervention), link them to a program that provides more intense interventions, such as those in the Compendium of Evidence-based HIV Prevention Interventions (see <http://www.cdc.gov/hiv/topics/research/prs/evidence-based-interventions.htm>) which are often provided by local health departments or community-based organizations. These patients may also be good candidates for continued use of PrEP until they are consistently practicing effective behavioral risk reduction.

- Counseling patients who test HIV-negative. Guidelines have emphasized the importance of risk-reduction counseling for persons determined to be at substantial risk of sexual HIV acquisition²⁷. It is recommended that you select the most appropriate brief sexual risk-reduction intervention that can address the immediate prevention needs of HIV-negative patients at substantial risk for acquiring HIV infection. One counseling approach designed for STD clinic providers, the RESPECT model²⁸, can be used. The model consists of two brief, 20-minute, interactive, patient-focused counseling sessions that are conducted during HIV testing, and have been found to significantly reduce sexual risk behaviors and prevent new STDs among HIV-negative patients (although not HIV incidence). Besides RESPECT, there are now several other effective brief sexual risk-reduction intervention models that should be considered when providing HIV-negative patients appropriate prevention counseling. Although no brief counseling models have

yet proven effective for patients taking PrEP, some of the models developed for persons with HIV infection, (Video Doctor²⁹, Partnership for Health³⁰, and motivational interviewing^{20,31}) may be appropriate for adaptation to counseling patients who are taking PrEP.

Intensive sexual risk reduction interventions may be appropriate for some patients, who should be referred to appropriate providers. In general, HIV risk-reduction interventions have been shown through numerous systematic reviews, to be efficacious in reducing HIV sexual risk behaviors, promoting protective behaviors, and reducing the incidence of new sexually transmitted infections among high-risk populations from various demographic, racial/ethnic, or behavioral risk groups³²⁻³⁵.

- Counseling patients who test HIV-positive. Provide emotional support and counseling to patients who receive preliminary or confirmed positive HIV test results to help them understand the test result, the benefits of initiating and remaining in HIV medical care, and the importance of reducing their HIV-related sexual and/or injection risk behaviors to help protect their health and the health of their partners. Link all HIV-positive patients to HIV medical care, prevention services that routinely offer risk screening and ongoing risk-reduction interventions, and other health services as needed.

PREP FOLLOW-UP VISITS

Provide brief behavioral HIV risk assessment and supportive counseling at each follow-up visit while the patient is taking PrEP medication. For important components of these sessions, see Box 7.1. At least annually discuss with the patient whether discontinuation of PrEP is warranted. If the decision is made to discontinue PrEP, a plan for periodic reassessment should be made and any indicated referrals to community programs or other support services should be arranged.

Box 7.1: Elements of brief HIV risk-reduction counseling in clinical settings

- Create and maintain a trusting and confidential environment for discussion of sexual or substance abuse behaviors.
- Build an ongoing dialogue with the patient regarding their risk behavior (and document presence or absence of risk behaviors in the confidential medical record).
- Reinforce the fact that PrEP is not always effective in preventing HIV infection particularly if used inconsistently, but that consistent use of PrEP together with other prevention methods (consistent condom use, discontinuing drug injection or never sharing injection equipment) confers very high levels of protection.

Section 9 PrEP-Related ICD, CPT and LOINC codes

ICD-9 codes	Description	ICD-10 codes	Description
V01	Contact with or exposure to communicable diseases	Z20	Contact with and (suspected) exposure to communicable diseases
		Z20.2	Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission
		Z20.5	Contact with and (suspected) exposure to viral hepatitis
		Z20.6	Contact with and (suspected) exposure to human immunodeficiency virus (HIV)
V01.7	Exposure to other viral diseases	Z20.82	Contact with and (suspected) exposure to other viral communicable diseases
V15.85	Exposure to potentially hazardous body fluid	Z77.21	Contact with and (suspected) exposure to potentially hazardous body fluids
E920.5	Needlestick	W46	Contact with hypodermic needle: “the appropriate 7 th character is to be added to each code from category W46” A- initial encounter, D- subsequent encounter, S- sequela
		W46.0	Contact with hypodermic needle (hypodermic needle stick NOS)
		W46.1	Contact with contaminated hypodermic needle
V01.8	Exposure to other communicable diseases	Z20.8	Contact with and (suspected) exposure to other communicable diseases
		Z20.81	Contact with and (suspected) exposure to other bacterial communicable diseases
V07.8	Other specified prophylactic measure	Z79	Long term (current) drug therapy. Includes long term (current) drug use for prophylactic purposes
		Z51.81	Therapeutic drug level monitoring
		Z51.89	Encounter for other specified aftercare
V07.9	Unspecified prophylactic measure	Z79.899	Other long term (current) drug therapy
042	Human immunodeficiency virus illness or disease with symptoms	B20	Human immunodeficiency virus (HIV) disease. Includes: AIDS; AIDS-related complex (ARC); HIV infection, symptomatic
V08	Human immunodeficiency virus infection , asymptomatic	Z21	Asymptomatic human immunodeficiency virus (HIV) infection status

ICD-9 codes	Description	ICD-10 codes	Description
070.30	Hepatitis, viral, type B (acute) without hepatic coma	B16.9	Acute hepatitis B without delta-agent and without hepatic coma
		B16.1	Acute hepatitis B with delta-agent without hepatic coma
V02.61	Hepatitis, viral, type B carrier status	B17.0	Acute delta-(super) infection of hepatitis B carrier
		Z22.51	Carrier of viral hepatitis B
070.32	Hepatitis, viral, type B, chronic	B18.0	Chronic viral hepatitis B with delta-agent
		B18.1	Chronic viral hepatitis B without delta-agent
070.31	Hepatitis, viral, type B, delta	B16.0	Acute hepatitis B with delta-agent with hepatic coma
		B16.2	Acute hepatitis B without delta-agent with hepatic coma
	<i>No current ICD-9 diagnosis code</i>	Z00.0	Encounter for general adult medical examination
		Z01.812	Encounter for preprocedural laboratory examination (blood and urine tests prior to treatment or procedure)
		Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission
		Z11.4	Encounter for screening for human immunodeficiency virus (HIV)
		Z11.59	Encounter for screening for other viral diseases
		Z11.8	Encounter for screening for other infectious and parasitic diseases
		Z13.89	Encounter for screening for other disorder (encounter for screening for genitourinary disorders)
		Z13.9	Encounter for screening unspecified
		Z32.0	Encounter for pregnancy test
		Z70.0	Counseling related to sexual attitude
		Z70.1	Counseling related to patient's sexual behavior and orientation
		Z70.3	Counseling related to sexual behavior and orientation of third party (child, partner, spouse)
		Z72.5	High risk sexual behavior
		Z72.51	High risk heterosexual behavior
Z72.52	High risk homosexual behavior		
Z72.53	High risk bisexual behavior		

Sources: <http://www.cdc.gov/nchs/icd/icd9cm.htm> and <http://www.cdc.gov/nchs/icd/icd10cm.htm>

CPT Codes	Description
4276F	Potent antiretroviral therapy prescribed (HIV)
4270F	Patient receiving potent antiretroviral therapy for ≥ 6 months (HIV)
4290F	Patient screened for injection drug use (HIV)
4293F	Patient screened for high-risk sexual behavior (HIV)
86701	HIV antibody test performed (HIV-1 only)
86703	HIV antibody test performed (HIV-1 and HIV-2)
87389	HIV-1 EIA antibody with HIV1&2 antigens
87390	HIV-1 detection by immunoassay (IAAD EIA HIV-1)
87534	HIV-1 detection by nucleic acid, direct probe
87535	HIV-1 detection by nucleic acid, amplified probe
87536	HIV-1 quantitation
87900	Infectious agent drug susceptibility phenotype prediction using regularly updated genotypic bioinformatics
87901	HIV-1 genotype by nucleic acid (RNA or DNA)
80074	Hepatitis panel
86704	HBcAb
86705	HBcAb, IgM antibody
87340	HBsAg
87517	Hepatitis B quantitation

Source: <http://online.statref.com/titleinfo/fxid-24.html>

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
0020025	Creatinine, Serum or Plasma	0020025	Creatinine, Serum or Plasma	2160-0
0020144	Renal Function Panel	0020025	Creatinine, Serum or Plasma	2160-0
0020399	Basic Metabolic Panel	0020025	Creatinine, Serum or Plasma	2160-0
0020408	Comprehensive Metabolic Panel	0020025	Creatinine, Serum or Plasma	2160-0
0085024	CTT Chemistry 20 Profile	0020025	Creatinine, Serum or Plasma	2160-0
0085025	CTT Chemistry 27 Profile	0020025	Creatinine, Serum or Plasma	2160-0
0020089	Hepatitis B Surface Ag w/ Reflex to Conf	0020089	Hepatitis B Surface Antigen	5196-1
0020090	Hepatitis B Virus Surface Antibody	0020090	Hepatitis B Surface Antibody	5193-8
0020091	Hepatitis B Virus Core Antibodies, Total	0020091	Hepatitis B Core Antibodies, Total	13952-7
0020092	Hepatitis B Virus Core Antibody, IgM	0020092	Hepatitis B Core Antibody, IgM	24113-3
0020128	Hepatitis B Virus Surface Ag, Confirm	0020128	Hepatitis B Surface Antigen Confirmation	7905-3
0020454	Hepatitis Panel, Chronic HBV	0020089	Hepatitis B Surface Antigen	5196-1
0020454	Hepatitis Panel, Chronic HBV	0020522	Chronic Hepatitis B Panel Interpretation	45159-1
0020454	Hepatitis Panel, Chronic HBV	0020090	Hepatitis B Surface Antibody	5193-8
0020457	Hepatitis Panel, Acute	0020092	Hepatitis B Core Antibody, IgM	24113-3
0020457	Hepatitis Panel, Acute	0020179	Acute Hepatitis Panel Interpretation	13169-8
0020457	Hepatitis Panel, Acute	0020089	Hepatitis B Surface Antigen	5196-1

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
0056025	Hepatitis B Virus DNA Quant RT- PCR	0051820	HBV DNA Interpretation	29610-3
0056025	Hepatitis B Virus DNA Quant RT- PCR	0056026	HBV DNA (log IU/mL)	48398-2
0056025	Hepatitis B Virus DNA Quant RT- PCR	2002322	HBV DNA (IU/mL)	42595-9
2001567	Hepatitis B Virus Genotype	2001569	Hepatitis B Genotype	32366-7
2001567	Hepatitis B Virus Genotype	2001569	Hepatitis B Genotype	32366-7
2006526	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2006611	HIV-1,2 Combo Antigen/Antibody	56888-1
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2007986	HIV Interpretation	69668-2
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2007982	HIV-1/HIV-2 Antibody Differentiation	42768-2
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2007985	_HIV-2 Antibody by Multispot	30361-0
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2007984	_HIV-1 Antibody by Multispot	29893-5
2007980	HIV-1,2 Combo Ag/Ab EIA w/Reflex	2007981	HIV 1,2 Combo Antigen/Antibody	56888-1
0020284	HIV 1 Antibody Confirm, Western blot	0020284	HIV-1 Antibody Confirm, Western blot	5221-7
0020698	HIV-1 Ab Confirm, Western blot w/Reflex	0020284	HIV-1 Antibody Confirm, Western blot	5221-7
2005375	HIV-1 w/Reflex to HIV-1 Western blot	2005376	HIV-1 Antibody	29893-5
0051250	HIV-2 Antibody w/Reflex to Supplemental	2008282	HIV-2 Antibody, Supplemental	30361-0
0051250	HIV-2 Antibody w/Reflex to	0051251	HIV-2 Antibody by ELISA	30361-0

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
	Supplemental			
0093061	HIV-1 PCR, Qualitative	0093062	HIV-1 PCR, Qualitative	44871-2
0093061	HIV-1 PCR, Qualitative	0093062	HIV-1 PCR, Qualitative	44871-2
0020466	HIV 1 RNA Quantitative by bDNA	0020464	HIV-1 RNA Quant bDNA, Log	29539-4
0020466	HIV 1 RNA Quantitative by bDNA	2002687	HIV-1 RNA Quant bDNA, Copy	23876-6
0055598	HIV-1 RNA Qnt By Real-Time PCR	0051817	HIV-1 RNA Qnt Real-Time PCR Interp	24013-5
0055598	HIV-1 RNA Qnt By Real-Time PCR	2002646	HIV-1 RNA Qnt Real-Time PCR, Copy	20447-9
0055598	HIV-1 RNA Qnt By Real-Time PCR	0020297	HIV-1 RNA Qnt Real-Time PCR, Log	29541-0
2002688	HIV-1 RNA Quant bDNA reflex to Genotype	0020464	HIV-1 RNA Quant bDNA, Log	29539-4
2002688	HIV-1 RNA Quant bDNA reflex to Genotype	2002687	HIV-1 RNA Quant bDNA, Copy	23876-6
2002689	HIV-1 RNA Quant reflex to Genotype	0051817	HIV-1 RNA Qnt Real-Time PCR Interp	24013-5
2002689	HIV-1 RNA Quant reflex to Genotype	2002646	HIV-1 RNA Qnt Real-Time PCR, Copy	20447-9
0051186	HIV 1, vircoTYPE	0055648	VircoType Information	45182-3
0051186	HIV 1, vircoTYPE	0055648	VircoType Information	45182-3
0055670	HIV-1 Genotyping	0051722	HIV-1 Genotyping	49659-6
0055670	HIV-1 Genotyping	2002141	EER HIV-1 Genotyping	11526-1
0055670	HIV-1 Genotyping	0051722	HIV-1 Genotyping	49659-6
0055670	HIV-1 Genotyping	2002141	EER HIV-1 Genotyping	11526-1

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
2004331	HIV GenoSure MG	0092073	Viral Load - RT	8251-1
2004331	HIV GenoSure MG	0092074	Viral Load Date - RT	19151-0

Source: <http://loinc.org/>

Section 10 Potential practice quality measures^{36,37}

Primary (Outcome) Measures

Quality Indicator	Eligible Population	Numerator	Denominator
HIV testing, baseline	All persons prescribed PrEP medication	Number of patients with negative HIV test result documented within 1 week prior to initial prescription of PrEP medication	Number of persons prescribed PrEP
HIV testing, interval	All persons prescribed PrEP medications	Number of PrEP patients with an HIV test result documented at least every 3 months while PrEP medication prescribed	Number of persons prescribed PrEP for >3 months continuously
PrEP Medication	All persons prescribed PrEP medications	Number of persons for whom the prescribed regimen matches CDC guidelines	Number of persons prescribed PrEP medication
Seroconversion	All persons prescribed PrEP medications	Number of patients with a confirmed HIV positive test result while PrEP medications prescribed	Number of persons prescribed PrEP medication for >1 month
Seroconversion, resistant virus	All persons prescribed PrEP medication who received a genotypic resistance test within 4 weeks after an HIV positive test result	Number of persons seroconverting while taking PrEP who have resistant virus detected by genotypic test	Number of persons prescribed PrEP medication who received a genotypic resistance test within 4 weeks after a confirmed HIV positive test result

Section 11 Methods for Developing the PrEP Clinical Practice Guideline

In 2009, in recognition of the lead time needed to develop clinical guidance for the safe and effective use of PrEP should clinical trials results support it, CDC initiated a formal guidelines development process to allow for early review of the relevant literature, discussion of potential guidelines content given scenarios of potential trial results, and fostering the development of expert and stakeholder consensus. This process was designed to provide a basis for the rapid issuance of interim guidance, to be followed by Public Health Service guidelines as soon as the earliest trial findings indicated sufficient PrEP efficacy and safety to merit its implementation for HIV prevention through one or more routes of transmission.

This guidelines development process was based on a review of experience with the development of other clinical and nonclinical guidelines at CDC, including those for STD treatment and antiretroviral prevention of mother-to-child transmission following the ACTG 076 trial results.

There were five basic components to the process for developing PrEP guidelines:

1. An **HHS Public Health Service (PHS) Working Group** to develop interagency consensus on major points of implementation policy and provide agency review of guidelines. This working group included representatives from agencies that would formally clear PHS guidelines (FDA, HRSA, NIH, HHS/OHAP) as well as agencies that may implement such guidance (IHS, VA).
2. A **CDC writing team** responsible for preparing draft guidance documents based on the recommendations of the other groups involved in the guidelines process
3. A number of **external work groups** responsible for considering specific sets of issues for the planned guidance. Each work group was composed of 5-8 members representative of the following:
 - Members of the academic community and scientists with expertise in the content area to ensure that the guideline elements are science-based
 - Health department and clinical users of the guidelines to ensure the feasibility of implementing guideline elements in local and state HIV prevention programs
 - At least one advocate or community-based organization member with personal or professional experience in the content area to serve as an ongoing bridge to community discussions and to supplement the advocate input received by other activities.
 - Geographic diversity (multiple US regions and small/medium/large jurisdictions)
 - Experience with PrEP issues when possible

External work groups were convened to consider the following areas:

- Clinical care guidance
- Clinic-based counseling guidance
- Integrating PrEP with other prevention services
- Persons potentially exposed by injection drug use
- MSM
- Women
- African American, Hispanic/Latino, and other heterosexual men
- Adolescents

In addition to these standing work groups, technical expert panels were convened to inform guidelines for PrEP use in the following areas:

- Public health and clinical ethics
 - Monitoring and evaluation framework
 - Financing and reimbursement issues
 - Preconception and intrapartum use of PrEP
 - Public health legal and regulatory issues
 - Issues relevant to benefits managers and insurers
4. A series of **stakeholder web/phone conferences** were held to receive input on questions, concerns, and preferences from a variety of perspectives including those of community-based organizations, state and local AIDS offices, professional associations, and others .
 5. After the publication of the first efficacy trial results, a **face-to-face consultation** of external experts, partners, agencies, and other stakeholders was held to consider the recommendations for guidance made by the above groups and to discuss any additional ideas for inclusion in PrEP guidelines.

This process allowed wide input, transparency in discussing the many issues involved, time for the evolution of awareness of PrEP and ideas for its possible implementation, in addition to facilitating the development of a consensus base for the eventual guidance. At the same time, it allowed for guidelines based on expert opinion, and recommendations deemed feasible by clinical providers and policymakers.

On the basis of results from the first 4 activities listed above and the publication in late November 2010 of results from the first clinical trial to show substantial efficacy and safety², CDC issued interim guidance for PrEP use among men who have sex with men in January 2011. This interim guidance was followed by a face-to-face meeting of external in May 2011. As efficacy and safety results were published, additional interim guidance documents were issued for heterosexually active adults (August 2012) and injection drug users (July 2013).

A draft guidelines document incorporated recommendations from participants in the development process and information gleaned from literature reviews, including PrEP clinical trial results. The draft also addressed guidelines standards for review of the strength of evidence (GRADE approach³⁸) as well as a format designed to promote guideline implementation (GLIA³⁹), dissemination (GEM⁴⁰), and adoption (AGREE^{41,42}).

The draft clinical practice guideline and providers supplement were reviewed by CDC, FDA, NIH, HRSA, and HHS, and a series of webinars were held in 2012 and 2013 to obtain additional expert opinion and public engagement on draft recommendations for PrEP use. The draft guideline and supplement were then reviewed by a panel of 6 external peer reviewers who had not been involved in their development. At each step, revisions were made in response to reviewer and public comments received.

PLANS FOR UPDATES TO THE GUIDELINE

PrEP is a rapidly changing field of HIV prevention with several additional clinical trials and studies are now underway or planned. Updates to these guidelines are anticipated as studies provide new information on PrEP efficacy, HIV testing, drug levels, adherence, longer term clinical safety, and changes in HIV risk behaviors associated with PrEP medication use for HIV uninfected MSM, heterosexuals, injection drug users, pregnant women and their newborns; as well as information on the efficacy and safety of other antiretroviral medications, and other routes and schedules of medication delivery.

When significant new data become available that may affect patient safety or new recommendations for PrEP use, a warning announcement with revised recommendations may be made on the CDC and *AIDSinfo* web sites until appropriate changes can be made in the guidelines document. Updated guidelines will be posted on the CDC (<http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf>) and *AIDSinfo* web sites (<http://www.aidsinfo.nih.gov>). The public will be given a 2-week period to submit comments about any revisions posted. These comments will be reviewed, and a determination made as to whether additional revisions are indicated.

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