

US PUBLIC HEALTH SERVICE

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE

CLINICAL PROVIDERS' SUPPLEMENT



What's New in the Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update – Clinical Providers' Supplement

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The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Providers' Supplement was published in an electronic format in July 2014 so that it could be updated as relevant changes in supporting evidence became available. The Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update – Clinical Providers' Supplement includes revisions to several sections. These revisions are intended solely to update the developing evidence base and to clarify specific points in clinical care.

- Checklist updated to include Descovy ,2-1-1 Truvada for MSM, and cabotegravir
- Added information about Descovy to Patient Information Sheet about Truvada
- Added a Patient Information Sheet about cabotegravir
- Restored a revised section on risk reduction counseling for clinicians
- Text specific to cabotegravir was added to several sections.
- Minor revisions were also made to correct typographical errors, add references, and update content from cited guidelines and source materials.

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For more clinical advice about PrEP guidelines:

- call the National Clinicians Consultation Center PrEPLine at **855-448-7737** or
- go to their website at <http://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/>
- go to the CDC HIV website for clinician resources at <https://www.cdc.gov/hiv/clinicians/index.html>

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Introduction

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 couples,⁴ 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) or tenofovir alafenamide (TAF) and emtricitabine (F).³

In addition, one clinical trial among persons who inject drugs (PWID) (also called injection drug users [IDU])⁶ and one among men and women in heterosexual HIV-discordant couples⁴ have demonstrated substantial efficacy and safety of daily oral PrEP with TDF alone. The demonstrated efficacy of daily oral 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), all of which were provided to trial participants, including persons in the drug treatment group and persons in the placebo group. In July 2012, after reviewing the available trial results, the U.S. Food and Drug Administration (FDA) approved an indication for the use of Truvada (F/TDF) “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.”⁷ In May 2018, the approval for F/TDF was extended to adolescents weighing at least 35 kg (77 lb) based on safety trials in adolescents⁸ and young adults.⁹ In June 2019, the US Preventive Services Task Force recommended PrEP for adults and adolescents at risk of HIV acquisition with an “A” rating (high certainty that the net benefit of the use of PrEP to reduce the risk of acquisition of HIV infection in persons at high risk of HIV infection is substantial).¹⁰ And in October 2019, based on a clinical trial conducted with 5,313 MSM and 74 transgender women, the FDA approved a PrEP indication for daily F/TAF for sexually active persons at risk of HIV acquisition.³ Women at risk through receptive vaginal sex were excluded from the F/TAF approval, because no women (assigned female sex at birth) were included in the efficacy and safety PrEP trial. In 2020, results from a clinical trial conducted with MSM and transgender women¹¹ and another conducted African women¹² reported high efficacy and safety for bimonthly injections of cabotegravir (CAB) for PrEP. Submission of data for review by the FDA for approval of a PrEP indication is planned in 2021.

On the basis of these trial results and FDA approvals, the U.S. Public Health Service published a comprehensive clinical practice guideline for the use of PrEP for the prevention of HIV infection in the United States in 2014 and updated it in 2017 and in 2020.

<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.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.

Many of the studies that informed these guidelines included small numbers of transgender women and none included transgender men, as a result, data specifically relevant for transgender and non-binary people are often limited or not available. Most sections of this supplement, therefore, use the terminology, ‘women’ and ‘men’ unless specifically referring to transgender women or men. We continue to advocate for greater inclusion of transgender and non-binary people in PrEP-related research and recommend gender-inclusive models of PrEP care to ensure that services encompass and address the needs of all persons who would benefit from its use.

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 as prescribed
- ☐ Information about PrEP use during conception and pregnancy (when indicated)
- ☐ The following PrEP regimen (choose only one)
 - ☐ Prescribed Truvada (300 mg tenofovir disoproxil fumarate, 200 mg emtricitabine)

daily dosing

- ☐ Prescribed Descovy (25 mg tenofovir alafenamide, 200 mg emtricitabine)

daily dosing (MSM)

- ☐ Prescribed Truvada (300 mg tenofovir disoproxil fumarate, 200 mg emtricitabine)

2-1-1 dosing (MSM)¹

- ☐ Administered a gluteal IM injection of cabotegravir (600 mg in 3 ml)
- ☐ A follow-up appointment date

As the provider, I will:

¹ An off-label use

- Limit refill periods to recommended intervals for repeat HIV testing
 - Daily dosing, Truvada or Descovy - (≤ 90 day supply)
 - 2-1-1 dosing (Truvada only, MSM only) ≤ 30 day supply)
- Assess HIV status (including signs or symptoms of acute HIV infection at
 - Every 3-month follow-up visit for those prescribed oral PrEP
 - Every other bimonthly follow-up visits (every 4 months) for those provided CAB injections
- Conduct follow-up visits for:
 - Assessment of side effects and advice on how to manage them
 - Assessment of STI symptoms, HIV risk behavior and counseling support for risk-reduction practices
 - Assessment of medication adherence for patients prescribed oral PrEP and counseling to support adherence
- Inform the patient of any new information about PrEP and respond to questions

Patient Section – Daily Oral Dosing
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It has been explained to me that:

- Taking a dose of PrEP medication every day will lower my risk of getting HIV infection.
- This medicine does not completely eliminate my risk of getting HIV infection and does not reduce my risk of getting a sexually transmitted infection, so using condoms during sex will provide additional protection.
- 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

Patient Section – “2-1-1” Dosing

It has been explained to me that:

- Taking the PrEP medication I have been prescribed (Truvada) both before and after I have sex every day can lower my risk of getting HIV infection.
- I should take 2 pills in the 2-24 hours before I expect to have sex, then 1 pill a day later, and 1 pill two days later.
- If I am having sex at least once a week, I should consider taking PrEP medication daily rather than before and after each time I have sex.
- This medicine does not completely eliminate my risk of getting HIV infection and does not reduce my risk of getting a sexually transmitted infection, so using condoms during sex will provide additional protection.
- 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 before and after each time I have sex.
- Talk to my provider about any problems I have in taking the medication before and after each time I have sex.
- Not share the medication with any other person.
- Attend all my scheduled appointments.
- Call _____ to reschedule any appointments I cannot attend.

Patient Section – Cabotegravir Injections

It has been explained to me that:

- Receiving the PrEP injections (cabotegravir) every 8 weeks will lower my risk of getting HIV infection.
- This medicine does not completely eliminate my risk of getting HIV infection and does not reduce my risk of getting a sexually transmitted infection, so using condoms during sex will provide additional protection.
- 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 4 months.

Therefore, I will:

- Attend all my scheduled appointments.
- Call _____ to reschedule any appointments I cannot attend.
- Talk to my provider if I want to stop taking PrEP injections so that I can stop safely

Give one copy to patient

Section 2 PrEP Information Sheet

Pre-exposure Prophylaxis (PrEP) for HIV Prevention

Frequently Asked Questions

What is PrEP?

“PrEP” stands for preexposure prophylaxis. 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 or by getting an injection with 1 HIV medicine every 2 months. These are the same medicines used to stop the virus from growing in people who already have HIV infection.

Why take PrEP?

Nearly 40,000 people get infected with HIV each year in the U.S. 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 medications that have been shown to be safe and to help block HIV infection are called “Truvada” (pronounced tru va duh) or “Descovy” (pronounced des koh vee). Truvada is a combination of 2 drugs (tenofovir disoproxil fumarate and emtricitabine). Descovy is a combination of 2 drugs (tenofovir alafenamide and emtricitabine). The drug in the injection is called cabotegravir (pronounced cab oh teh gruh veer). These medicines work by blocking important pathways that the HIV virus uses to set up an infection. If you take either of these medications 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 pills in the way you were instructed, there may not be enough medicine in your blood stream to stop the virus from establishing an infection in your body.

Should I consider taking daily PrEP?

PrEP is not for everyone. 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 and does not have his/her virus under control with medication. 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 injects 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 and women at high risk of being exposed to HIV while having sex or injecting drugs. 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 or an injection every other month, (3) received intensive counseling on safer-sex and safe-injection behavior, (4) were tested regularly for sexually transmitted infections, and (5) were given a regular supply of condoms.

In these studies, when people took PrEP daily (or missed only occasional doses) or had regular PrEP injections, the risk of getting HIV infection during sex dropped by 90% or more. When people who used PrEP in the community were assessed, the risk of getting HIV infection during sex dropped by up to 99%. People who take PrEP daily as prescribed rarely get 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 of oral PrEP medicines had early side effects such as an upset stomach or loss of appetite, but these side effects were mild and usually went away within the first month. Some people also had a mild headache. Many people in trials of PrEP injections had a reaction at the injection site like mild pain, redness, or swelling. These reactions were mild and lasted only a couple of days. No serious side effects were observed. You should tell your health care provider 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 provider about PrEP. If you and your health care provider 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. For oral PrEP, your blood will also be tested to see if your kidneys 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 health care provider will give you the form of PrEP you decide on; either a prescription for an oral pill (Truvada or Descovy) or an injection with cabotegravir.

Taking PrEP medicines will require you to follow-up regularly with your health care provider. You will receive counseling on sexual behaviors and blood tests for HIV infection and to see if your body is reacting well to Truvada, Descovy, or cabotegravir. You should take your oral medicine daily as prescribed or your injections every two months, and your health care provider 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 health care provider if you are having trouble remembering to take your medicine, return for your injections, or if you want to stop PrEP.

Is daily Truvada my only choice for PrEP?

If you are a man who has sex with men (MSM) or a transgender woman, there is a second option for taking daily PrEP. A large study of MSM showed that daily use of a second medication called Descovy, is just as safe and effective as Truvada. Since Descovy was not studied in persons assigned female sex at birth, it is unknown whether it is effective protection for vaginal sex. So, it should only be prescribed to MSM. An additional trial has shown that injections with cabotegravir every two months is highly effective HIV prevention.

Is taking medication every day my only choice for PrEP?

Another large study with MSM showed that for men who have sex infrequently, Truvada can be highly protective when taken only before and after sex. Among men who could anticipate when they would have sex, they took two pills several hours before having sex on a given day, then one pill a day later, and a final pill the next day. Because of this schedule of pill taking, it's called "2-1-1" PrEP. This was only studied with Truvada taken by MSM, so 2-1-1 PrEP is NOT prescribed for women or with Descovy, because we do not know it will work well. An additional trial has shown that injections with cabotegravir every two months is highly effective HIV prevention.

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 health care provider. 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. You can restart PrEP later if your life changes in ways that increase your risk. If you find you don't want to take a pill every day or often forget to take your pills, or don't want to continue PrEP injections, 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 health care provider may stop prescribing PrEP for you.

Do I need to do anything special if I want to stop having PrEP injections?

If you stop taking PrEP pills, the medication clears from your body within a couple of weeks. But when you stop receiving PrEP injections, the medication takes a year or more to completely leave your body (sometimes called the “tail” period). As the level of medication drops, protection drops and you can get HIV if you are exposed to it. If you have low levels of medication and get HIV, the virus can be less sensitive to the medication (“resistant”) and this might effect which medications would treat your infection. For that reason, it is important to have effective protection against HIV during the months while the cabotegravir is gradually leaving your body. This may mean you need to take daily oral PrEP medication for several months. It is important to make a plan with your provider for protection during this period.

Section 3 Medication Information Sheets

Truvada and Descovy Medication Information Sheet for Patients

Brand name: Truvada (tru va duh), Descovy (des koh vee)

Generic name: tenofovir disoproxil fumarate and emtricitabine, tenofovir alafenamide and emtricitabine

Why is this medication prescribed?

- Truvada and Descovy are two of several medications that are currently used to *treat* human immunodeficiency virus (HIV)
- Truvada and Descovy are now being also used to prevent HIV infection.
- Truvada and Descovy are 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 or Descovy to prevent HIV infection, health care providers refer to this use as “pre-exposure prophylaxis” or “PrEP.”
- Descovy is not prescribed for women (persons assigned female at birth).

How does PrEP medication help prevent HIV infection?

- HIV is a virus that attacks your body’s immune cells (the cells that work to fight infections).
- Truvada and Descovy each contain a different form of tenofovir. They work against HIV in the same way so patients can take either medication (but not both).
- The 2 medications that make up Truvada and Descovy (tenofovir and emtricitabine) block important pathways that viruses use to set up infection.
- If you take Truvada or Descovy as PrEP daily, the presence of the medication in your bloodstream will usually stop the virus from establishing itself and slow the spread of HIV in your body.

- PrEP with Truvada or Descovy does not work all the time so you should also use condoms during sex for the most protection from HIV and other sexually transmitted infections.

How should this medicine be used?

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

What special precautions should I follow?

Before taking Truvada or Descovy, you must do the following:

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

What special dietary instructions should I follow?

- Continue your normal diet unless your health care provider 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
- a small weight gain
- a change in the amount of some types of fats (lipids) in your blood

These side effects usually fade during the first month of taking PrEP medication. Tell your health care provider if any of these symptoms are severe or do not go away.

Truvada or Descovy may cause other effects on your health. Some effects can be serious. Call your health care provider 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 health care provider 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 or Descovy in my home?

- You should keep medication in the container it came in, or in a tightly closed pill container, 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 health care provider or if you are admitted to a hospital. Keep it with you always in case of emergencies.

Cabotegravir Medication Information Sheet for Patients

Brand name: cabotegravir (cab oh teh gruh veer)

Generic name: cabotegravir

Why is this medication prescribed?

- Cabotegravir is one of several medications that are currently used to *treat* human immunodeficiency virus (HIV)
- Cabotegravir is now being also used to prevent HIV infection.
- Cabotegravir injections are sometimes given 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) to help reduce their chances of getting HIV.
- When you take cabotegravir to prevent HIV infection, healthcare providers refer to this use as “pre-exposure prophylaxis” or “PrEP.”

How does PrEP medication help prevent HIV infection?

- HIV is a virus that attacks your body’s immune cells (the cells that work to fight infections).
- Cabotegravir works against HIV by blocking important pathways that viruses use to set up infection.
- If you take cabotegravir injections for PrEP, the presence of the medication in your bloodstream will usually stop the virus from establishing itself and slow the spread of HIV in your body.
- PrEP with cabotegravir does not work all the time so you should also use condoms during sex for the most protection from HIV and other sexually transmitted infections.

How should this medicine be used?

- You will receive a cabotegravir injection into the buttock muscle in the back side of your hip.
- Ask your health care provider or nurse to explain any part of PrEP use that you do not understand.
- Do not stop taking cabotegravir injections without talking to your health care provider.
- You will be at risk of getting HIV if you stop taking PrEP injections without starting another effective prevention method.

What special precautions should I follow?

Before getting a cabotegravir injection, you must do the following:

- Tell your health care provider and pharmacist about all prescription and nonprescription medications (e.g., vitamins, nutritional supplements, and herbal products), you are taking.

Your health care provider may need this information to know if any of these medicines interact with the cabotegravir.

- Tell your health care provider if you become pregnant or if you are breastfeeding.

What special dietary instructions should I follow?

- Continue your normal diet unless your health care provider tells you otherwise.

What should I do if I forget my appointment for an injection?

- If you miss an injection appointment, schedule another visit to continue injections.

What side effects can this medication cause?

You may experience the following side effects at the site where you got your cabotegravir injection:

- mild or moderate pain
- redness
- local swelling

These side effects usually fade within a few days of your PrEP injection. Taking an over-the-counter pain medication and using a heating pad at the site of the injection for 15-20 minutes a couple of times each day may help reduce the reaction. Tell your health care provider if any of these symptoms are severe or do not go away.

If you experience a serious side effect, you or your health care provider 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).

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 spreads 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 health care provider 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 health care provider 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 will be changed to another medication 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, also known as resistant virus. So, finding out quickly that you have HIV infection and changing to a more effective medication can protect your long-term health and keep your treatment options open.

Lastly, 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 HIV. 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 could more easily pass the virus to others. 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 2 or more medicines that fight HIV. Nearly all health care providers start people on treatment medications as soon as HIV tests show they have gotten the virus. Treatment also reduces the chances that a person with HIV infection will transmit the virus to his/her sex partners. When treatment is able to reduce the amount of HIV in your blood to a level too low to be measured (also called "undetectable"), there is effectively no risk of passing the virus to another person during sex.

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

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

Second, discuss with your health care provider 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 Risk Reduction Counseling

Assessing HIV and STI risk should be a part of every initial and follow-up PrEP visit. Based on the risks identified for a patient's potential exposure to HIV, you should encourage risk reduction by providing prevention counseling whether the patient will be prescribed PrEP or not.

Prevention counseling is most effective if provided in a nonjudgmental and empathetic manner appropriate to the patient's culture, language, sex and gender identity, sexual orientation, age, and developmental level. USPSTF recommends intensive behavioral counseling for all sexually active adolescents and for adults at increased risk for STIs and HIV.

For patients being prescribed PrEP, they will be utilizing the most effective HIV risk reduction method available. Educating the patient on how to ensure PrEP is maximally effective and supporting adherence to PrEP should be prioritized. Following that, you should provide science-based information on other HIV and STI prevention methods such as condoms, reducing the number of sexual partners, knowing their partner's HIV status, understanding the benefits of an HIV partner being on treatment with an undetectable viral load, and strategies to reduce the effect of alcohol or drug use on sexual risk taking. The goal should be to provide the patient with the necessary information for them to decide which prevention strategies they consider achievable and valuable.

Having a risk-reduction conversation can be challenging. The conversation often takes time and behavioral change in any patient can be slow. For PrEP patients who will be regularly monitored, you will have time to build a relationship with the patient during regular follow-up visits. These follow-up visits offer opportunities for an ongoing discussion of HIV risk including ways the patient could further reduce their risk. Critical to building a respectful relationship is to approach the conversation without judgement. The goal is to develop a risk reduction plan that meets the patient's needs while keeping their risk as low as possible. Some patients will not make the objectively safest choice or the choice that you believe is best. In these situations, you have to be prepared to accept and support the patient's decisions, and continue to provide non-judgmental, evidence-based information. At each subsequent visit, reassess the patient's risk, ask about other risk reduction measures they have taken, their successes and what barriers they may have

encountered. Offer support for any risk-reduction efforts taken and provide advice on additional or other risk reduction measures the patient should consider.

Training in client-centered counseling and motivational interviewing is available through:

- National Network of Clinical Prevention Training Centers (<https://www.nnptc.org>)
- National HIV Classroom Learning Center (<https://www.caiglobal.org>)
- CDC Train (<https://www.train.org/cdctrain/welcome>)

CDC provides information on effective behavioral risk reduction interventions

- Compendium of Evidence-based Interventions and Best Practices for HIV Prevention (<https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html>)

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 acquiring HIV infection.

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

MSM Risk Index¹³

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 when he did not use 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) with a man who was HIV- positive when you did not use a condom?	If 5 or more times, score 6	
		If 0-4 times, score 0	_____

MSM Risk Index¹³

6	In the last 6 months, have you used methamphetamines such as crystal or speed?	If yes, score 6	
		If no, score 0	_____
		Add down entries in right column to calculate total score	_____
			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 PWID (IDU) 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 acquiring HIV infection.

This section contains a tool that clinicians can use to quickly and systematically determine which persons who inject drugs (PWID) (also called injection drug users [IDU]) are at high risk for acquiring HIV infection and for whom PrEP may be indicated.

PWID (IDU) Risk Index ¹⁴				
1	How old are you today (in years)?		If <30 years, score 38 If 30- 39 years, score 24 If 40-49 years, score 7 If ≥50 years, score 0	_____
2	In the last 6 months, were you in a methadone maintenance program?		If yes, score 0 If no, score 31	_____
3	In the last 6 months, how often did you inject heroin?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you inject cocaine?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share a cooker?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you share needles?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
	In the last 6 months, how often did you visit a shooting gallery?	If 1 or more times, If 0 times,	Injection sub-score 1 Injection sub-score 0	_____
Add the five injection subscores to obtain a Composite Injection Subscore		If sum of five injection subscores is; 0 1 2 3 4 5	then Composite Injection Score is: 0 7 21 24 24 31	_____
Add the scores for age and methadone use to the Composite Injection Subscore to yield a Total Score				_____ Total Score*

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Section 8 Management of Patients Who Acquire HIV While on PrEP

Patients who are being prescribed PrEP might acquire HIV infection for several reasons. When HIV infection is detected at the first follow-up visit after PrEP initiation, it can indicate that the patient had undetected acute infection when PrEP was initiated. When infection is detected at later follow-up visits, as it most commonly occurs, it might be because patients have stopped taking PrEP, have been taking it infrequently, or have been stopping and restarting it without retesting for HIV infection before restarting. Rarely, despite high adherence to continuous daily dosing, patients taking PrEP have acquired HIV infection. Infection while taking PrEP as prescribed can occur because of exposure to a drug-resistant viral strain¹⁵ or simply because, even with daily use, PrEP protection is high but not 100%.¹⁶

In all cases, when an HIV test during a follow-up visit indicates possible infection in a PrEP patient, the following steps should be taken:

- Counsel the patient about their HIV status and the resulting management plan:
 - If a single rapid antibody blood test was positive, explain the need to confirm presumptive HIV-positive status with laboratory testing.
 - If a rapid 4th generation (antigen/antibody) blood test was positive, explain high likelihood of HIV infection that will need to be confirmed with additional laboratory testing.
 - If a positive HIV test was based on laboratory testing with confirmatory results already known, explain certainty of HIV diagnosis.
 - Ask about signs and symptoms of acute infection since last clinic visit as well as PrEP medication adherence history.
- Conduct confirmatory HIV testing (if not completed already) and supplemental tests, if indicated:
 - If one or more rapid tests were positive, draw blood for confirmatory laboratory-based HIV testing with adequate blood for reflex HIV viral load testing if confirmed to be HIV infected.
 - If laboratory-based testing was positive, draw blood for HIV viral load, CD4 cell count, and HIV resistance testing.
 - For persons with confirmed HIV infection, conduct the following supplemental testing indicated for initiation of HIV treatment, including but not necessarily limited to the following:³²
 - Chemistry screen, ALT, AST, bilirubin, CBC with differential, urinalysis, and pregnancy test (in people of childbearing potential).
 - Fasting lipid profile, glucose, and hemoglobin A1c are also indicated, on the day that seroconversion is detected, if possible.
- Convert the PrEP regimen to an HIV treatment regimen recommended by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents.¹⁷

- It is not necessary to stop antiretrovirals entirely while waiting for additional laboratory test results. In the most likely event that the patient has HIV infection, immediate initiation of HIV treatment is indicated. Select from among the regimens recommended in the DHHS treatment guidelines.¹⁷
 - If the patient is taking oral PrEP
 - Continue the prescription of Truvada (TDF 300 mg/FTC 200 mg) once daily, pending results of resistance tests.
 - Add a third medication according to criteria in the section on “Recommended Initial Regimens for Most People with HIV” in the DHHS treatment guidelines.¹⁷
 - If the patient is receiving CAB injections:
 - Initiate a treatment regimen according to criteria in the section on “Recommended Initial Regimens for Most People with HIV” in the DHHS treatment guidelines.¹⁷

Do not hold initiation of treatment while waiting for results of resistance tests.

Consultation with an HIV specialist may be obtained by calling the toll-free national PrEPline at 855-448-7737.

In cases where a viral strain with significant resistance to tenofovir or cabotegravir is later identified, the regimen can then be optimized. In cases where HIV infection is not confirmed, the patient can be returned to a PrEP regimen..

- Provide client education about time to viral load suppression and treatment as prevention:
 - Reinforce the importance of medication adherence for the patient’s long-term health.
 - Discuss the importance of condom use to protect sexual partners and provide condoms.
 - Offer HIV testing for sex and drug injection partners and assistance with disclosure, if desired.
 - Ask if the patient had condomless sex or shared injection equipment during the past 72 hours, and if yes, offer nPEP for exposed partners.
- Consult with and transfer care to an experienced HIV care provider, if necessary.
 - Clinicians can call the National Clinical Consultation Center toll-free at (800) 933-3413.
- Discuss or complete insurance paperwork necessary for coverage of treatment medication.
 - Patients who are receiving medication through PrEP-specific medication assistance programs will need to switch to an HIV treatment assistance program.
 - Public or private insurance plans will generally not require additional paperwork but prior authorizations for PrEP may raise questions when switching to a prescription for a treatment regimen.
- Schedule follow-up visits, including social services, if required.
- Complete an HIV case report for the health department (completion of fields related to PrEP use at the time of seroconversion is highlighted in red below).

HIV Antiretroviral Use History (record all dates as mm/dd/yyyy)

Main source of antiretroviral (ARV) use information (select one) <input type="checkbox"/> Patient Interview <input type="checkbox"/> Medical Record Review <input type="checkbox"/> Provider Report <input type="checkbox"/> NHM&E <input type="checkbox"/> Other		Date patient reported information __/__/__
Ever taken any ARVs? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown		
If yes, reason for ARV use (select all that apply)		
<input type="checkbox"/> HIV Tx	ARV medications _____	Date began __/__/__ Date of last use __/__/__
<input checked="" type="checkbox"/> PrEP	ARV medications <u>Truvada or Descovy or Cabotegravir</u>	Date began <u>__/__/__</u> Date of last use <u>__/__/__</u>
<input type="checkbox"/> PEP	ARV medications _____	Date began __/__/__ Date of last use __/__/__
<input type="checkbox"/> PMTCT	ARV medications _____	Date began __/__/__ Date of last use __/__/__
<input type="checkbox"/> HBV Tx	ARV medications _____	Date began __/__/__ Date of last use __/__/__
<input type="checkbox"/> Other _____		
	ARV medications _____	Date began __/__/__ Date of last use __/__/__

HIV Testing History (record all dates as mm/dd/yyyy)

Main source of testing history information (select one) <input type="checkbox"/> Patient Interview <input type="checkbox"/> Medical Record Review <input type="checkbox"/> Provider Report <input type="checkbox"/> NHM&E <input type="checkbox"/> Other		Date patient reported information __/__/__
Ever had previous positive HIV test? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown		Date of first positive HIV test __/__/__
Ever had a negative HIV test? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown		Date of last negative HIV test (if date is from a lab test with test type enter in Lab Data section) __/__/__
Number of negative HIV tests within 24 months before first positive test = _____ <input type="checkbox"/> Unknown		

Section 9 Transition of Patients From Nonoccupational Postexposure Prophylaxis (nPEP) to Preexposure Prophylaxis (PrEP)

Two types of patients may be considered candidates for PrEP use after a course of nonoccupational postexposure prophylaxis (nPEP):

- Patients who request PrEP and also have had a possible sexual or injection drug-related HIV exposure in the prior 72 hours (i.e., are within the recommended window to start nPEP); or
- Patients who request repeated courses of nPEP, particularly over a relatively recent period (e.g., more than twice during the past 6 months).

If evaluation demonstrates nPEP is clinically indicated and that the patient is also eligible for PrEP (e.g., behavioral risk for repeated HIV exposure, recent bacterial STI diagnosis in a sexually active person), then these patients should both be provided a 28-day course of nPEP and be evaluated for transition to PrEP at the conclusion of their nPEP course.

TRANSITIONING IMMEDIATELY FROM NPEP TO PREP

Transitioning from nPEP to PrEP without interruption at the completion of the 28-day nPEP course has the advantages of (1) maintaining satisfactory antiretroviral drug levels for PrEP (if nPEP adherence has been good); and (2) maximizing continuous prevention measures through continuity of nPEP to PrEP care. Essential steps include:

- At conclusion of 28 days of nPEP:
 - Repeat a rapid HIV test (ideally with a fourth-generation antigen/antibody assay) and assess for signs and symptoms of acute HIV infection.
 - If the rapid HIV test is positive or suspicion exists of possible acute HIV infection, draw blood for confirmatory testing and continue a 3-drug nPEP regimen pending confirmation of HIV status.
 - If HIV infection is confirmed, see Section 7 of Clinical Providers' Supplement for indicated next steps.
 - If the rapid HIV test is negative and no signs or symptoms of acute infection exist:
 - Replace the nPEP regimen with either
 - F/TDF daily as PrEP
 - F/TAF daily as PrEP or
 - Cabotegravir bimonthly injections
 - Complete any PrEP baseline laboratory testing not already performed as part of nPEP testing.

- Provide medication adherence and risk-reduction support counseling.
- Complete any insurance/medication assistance paperwork required to cover PrEP medications (might be different than nPEP medications).
- Schedule follow-up visits for HIV, STI, and other laboratory testing, as well as medication refills, on the basis of standard PrEP clinical practice guidelines recommendations.

INITIATING PREP AT A LATER TIME

Deferring initiation of PrEP use can increase the period of risk for HIV acquisition, because patients are left without the benefit of protective antiretroviral use. However, for some patients concluding a course of nPEP, additional time is needed to: (1) make a decision about PrEP use; (2) perform additional clinical assessment and engage the patient in shared decision making in special medical circumstances, such as renal or liver impairment, pregnancy or breastfeeding; or (3) arrange and ensure coverage of medication costs, availability of continuity of PrEP care, or other logistic factors. Essential steps with this approach include:

- Reinforce the critical nature of safer sexual or injection drug use strategies while pending PrEP initiation;
- Obtain baseline testing per PrEP guidelines; and
- Initiate PrEP, when possible.

Consultation

Consultation with local or regional experts in nPEP and PrEP, or with the toll-free national PrEPline at 855-448-7737 or PEPlines at 888-448-4911, can be sought for clinical scenarios requiring additional information or management options.

Section 10 PrEP-Related ICD, CPT and LOINC codes

See also: <https://www.nastad.org/resource/billing-coding-guide-hiv-prevention>

ICD-10 codes	Description
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)
Z20.828	Contact with and (suspected) exposure to other viral communicable diseases
Z77.21	Contact with and (suspected) exposure to potentially hazardous body fluids
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
Z20.8	Contact with and (suspected) exposure to other communicable diseases
Z20.81	Contact with and (suspected) exposure to other bacterial communicable diseases
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
Z79.899	Other long term (current) drug therapy
B20	Human immunodeficiency virus (HIV) disease. Includes: AIDS; AIDS-related complex (ARC); HIV infection, symptomatic

ICD-10 codes	Description
Z21	Asymptomatic human immunodeficiency virus (HIV) infection status
B16.9	Acute hepatitis B without delta-agent and without hepatic coma
B16.1	Acute hepatitis B with delta-agent without hepatic coma
B17.0	Acute delta-(super) infection of hepatitis B carrier
Z22.51	Carrier of viral hepatitis B
B18.0	Chronic viral hepatitis B with delta-agent
B18.1	Chronic viral hepatitis B without delta-agent
B16.0	Acute hepatitis B with delta-agent with hepatic coma
B16.2	Acute hepatitis B without delta-agent with hepatic coma
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

ICD-10 codes	Description
Z72.51	High risk heterosexual behavior
Z72.52	High risk homosexual behavior
Z72.53	High risk bisexual behavior
Z79.899	Other long term (current) drug therapy

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

CPT Codes	Description
87340	HBsAg
87517	Hepatitis B quantitation
80375	Tenofovir-DP in urine or dried blood spot (Drug(s) or substance(s), definitive, qualitative or quantitative, not otherwise specified)
96372	Therapeutic, prophylactic, or diagnostic injection

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

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
0020457	Hepatitis Panel, Acute	0020179	Acute Hepatitis Panel Interpretation	13169-8
0020457	Hepatitis Panel, Acute	0020089	Hepatitis B Surface Antigen	5196-1
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

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
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 Supplemental	0051251	HIV-2 Antibody by ELISA	30361-0
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

LOINC Codes				
Order Test Number	Order Test Name	Result Test Number	Result Test Name	Result LOINC Code
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
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 11 Potential Practice Quality Measures^{37,38}

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 (F/TDF or F/TAF) or every 4 months (CAB) while PrEP medication prescribed	Number of persons prescribed PrEP for >3 months continuously
PrEP medication adherence	All persons prescribed PrEP medications	Number of PrEP patients with adherence assessment noted in the medical record for any visits when prescribed PrEP medication	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 12 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 gathering information and understanding the perspectives of experts and stakeholders. 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 guidelines 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 the 2014 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, including FDA, HRSA, NIH, HHS/OHAP, as well as agencies that may implement such guidance, including IHS and 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); and
 - 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; and

- 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; and
 - 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 the perspectives 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.

The 2017 and 2021 updates to the guidelines and supplement were based on systematic literature reviews and the work of a CDC writing team.

PARTICIPANTS IN PREP GUIDELINES DEVELOPMENT AND REVIEW

2014 CDC PrEP Guidelines Project Manager: Dawn K. Smith, MD, MS, MPH; National Center for HIV, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Centers for Disease Control and Prevention (CDC), Atlanta, GA

2014 CDC PrEP Guidelines Writing Team

Dawn K. Smith, MD, MS, MPH; Linda J. Koenig, PhD; Michael Martin, MD; Gordon Mansergh, PhD; Walid Heneine, PhD; Steven Ethridge, BS, MT; Marie Morgan; Jonathan Mermin, MD, MPH; Kevin Fenton, MD, PhD, FFPH; NCHHSTP, CDC, Atlanta, GA

2014 CDC PrEP Guidelines Reviewers

Kathleen Irwin, MD; Paul Weidle, PharmD, MPH; Taraz Samandari, MD, PhD; Bernard Branson, MD

2014 Federal Agency PrEP Guidelines Working Group:

Ronald Valdiserri, MD, MPH, Health and Human Services; Laura Cheever, MD, HRSA; Kimberly Struble, PharmD, FDA; Maggie Czarnagorski, MD, VA; David Burns, MD, NIH; Christopher Bates, HHS; Susan Moskosky, MS, RNC, OPA; Jack Stein, Ph.D, ONDCP; Heather Huentelman, PharmD, IHS; Seiji Hayashi, MD, MPH, HRSA; Karen Hench, RN, MS, HRSA; David Lanier, PhD, AHRQ, Amy Lansky, PhD, MPH, CDC

External Consultants:

The working groups and expert panels listed here were convened by teleconference before trial results were available (2009-2010) and some were reconvened after each trial results for each population group were published. As technical experts, prevention partners, and key stakeholders, they were asked to assist in identifying relevant scientific/medical literature and share thoughts on topics that would inform the development of possible future guidelines for PrEP use in the US. They did not participate in the writing of these guidelines. No financial disclosures were sought. See Clinical Providers' Supplement section 14 for a description of the criteria use for constitution of the working groups and expert panels. Institutional associations listed for participants are those at the time of the group discussions and may have changed since.

Clinical care guidance WG: Myron Cohen, MD, UNC, Chapel Hill, NC; Craig Hendrix, MD, Johns Hopkins, Baltimore, MD; Bob Grant, MD, MPH, UCSF, San Francisco, CA; John Mellors, MD, U Pitt, Pittsburgh, PA; Anne Burns, American Pharmacists Association, Washington, DC; Keith Rawlings, MD, AIDS Arms Peabody Health Center, Dallas, TX; Grace Alfonsi, MD, HIV/STD Prevention Training Center of Denver Health and Hospital Authority, Denver, CO; Ryan Clary, Project Inform, San Francisco, CA.

Clinic-based counseling guidance WG: Kevin Malotte, DrPH, MA, CSU, Long Beach, CA; David Bangsberg, MD, MPH, Harvard, Boston, MA; James Dilley, MD, UCSF, San Francisco, CA; Lydia O'Donnell, Ed.D, Education Development Center, Newton, MA; Jeff Fisher, PhD, UConn, Storrs, CT; Mark Thrun, MD, Denver Health and Hospital Authority, Denver, CO; Richard Elion, MD, Whitman Walker, Washington, DC

Integrating PrEP with other prevention services: Tom Coates, PhD, UCLA, Los Angeles, CA; Grant Colfax, MD, SFDPH, San Francisco, CA; Lisa Longfellow, MPH, OPH-DHHS, New Orleans, LA; Marlene McNeese-Ward, Houston DHHS, Houston, TX; Ward Cates, MD, MPH, FHI, Research Triangle Park, NC; David Kern, NASTAD, Washington, DC; Johnnie Lee, MD, MPH, NACCHO, Stamford, CT; Marjorie Hill, PhD, GMHC, New York, NY; Kevin Fisher, JD, MSc, AVAC, New York, NY

Persons potentially exposed by injection drug use WG: Shruti Mehta, PhD, MPH, Johns Hopkins, Baltimore, MD; Crystal Fuller, PhD, MPH, Columbia University, New York, NY; Rich Needle, PhD, MPH, Pangaea Foundation, Oakland, CA; Steffanie Strathdee, PhD, UC- San Diego, San Diego, CA, ; Lisa Metsch, PhD, U Miami, Miami, FL; Daniel Raymond, Harm Reduction Coalition, New York, NY

MSM WG: Harvey Makadon, MD, Harvard, Boston, MA; Rafael Diaz, PhD, MSW, San Francisco State U, San Francisco, CA; Guillermo Chacón, Latino Commission on AIDS, New York, NY; Beau Gratzner, MPP, Howard Brown Health Center, Chicago, IL; Walt Senterfitt, PhD, CHAMP, Los Angeles, CA;

African American, Hispanic, and other heterosexual men WG: Carlos Del Rio, MD, Emory, Atlanta, GA; Shari Dworkin, PhD, MS, UCSF, San Francisco, CA; Amy Wohl, PhD, UCLA, Los Angeles, CA; Wayne

Duffus, MD, PhD, S Carolina HD, Columbia, SC; Oscar de La O, Bienestar, Los Angeles, CA; Leandro Mena, MD, MPH, U. Mississippi, Jackson, MS

Women's WG: Waafa El-Sadr, MD, MPH, MPA, Columbia, New York, NY; Gina Wingood, ScD, MPH, Emory, Atlanta, GA; Ada Adimora, MD, MPH, UNC, Chapel Hill, NC; Jo Schneiderman, Twin States Network & National Women and AIDS Collective (NWAC), Brattleboro, VT; Anna Forbes, MSS, Global Campaign for Microbicides, Washington, DC; Dazon Dixon-Diallo, MPH, SisterLove, Atlanta, GA

Adolescents WG: Isa Fernandez, PhD, U Miami, Miami, FL; Ralph DiClemente, PhD, MS, Emory, Atlanta, GA; Susan Kegeles, PhD, UCSF, San Francisco, CA ; Jennifer Augustine, MPH, CHES, Advocates for Youth, Washington, DC; Kristen McFee, MA, Alliance for Families and Children, Lynchburg, VA

Public Health Ethics Expert Panel: Bernard Lo, MD, UCSF, San Francisco, CA; Dan Brock, PhD, Harvard, Boston, MA; Robert Levine, MD, Yale, New Haven, CT; Scott Burris, JD, Temple, Philadelphia, PA; Kevin Cranston, MDiv, MA Dept. of Public Health, Boston, MA; Sean Philpott, PhD, MSB, UGC-Mt. Sinai, Schenectady, NY; Kate MacQueen, PhD, FHI, Research Triangle Park, NC; Mary Ann Chiasson, DrPH, Public Health Solutions, New York, NY; David Malebranche, MD, MPH, Emory, Atlanta, GA; Steven Wakefield, HVTN, Seattle, WA

Monitoring and Evaluation Expert Panel: Peter Kerndt, MD, MPH, LAC HD, Los Angeles, CA; Ted Palen, MD, PhD, MSPH, Kaiser Permanente, Denver, CO; Robert Heimer, PhD, MSc, Yale, New Haven, CT; Sandra Huang, MD, SF DPH, San Francisco, CA; Paul Aaron, FL DOH, Tallahassee, FL; Lucia Torian, PhD, NYC DOH, New York, NY; Neil Abernethy, PhD, UW, Seattle, WA; Ann Robbins, PhD, TX Dept of State Health Services, Austin, TX; Will Wong, MD, Chicago DPH, Chicago, IL; Cort Lohff, MD, MPH, VT DOH, Burlington, VT; Claudia Richards, MSW, SAMHSA, Rockville, MD; Nick Reuter, MPH, SAMHSA, Rockville, MD

Financing and Reimbursement Strategies Expert Panel: Jay Laudato, NYS Health Department, New York, NY; Jennifer Kates, MA, MPA, Kaiser Family Foundation, Washington, DC; Hugh Waters, PhD, Johns Hopkins, Baltimore, MD; Christine Lubinski, IDSA/HIVMA, Washington, DC; Eva Hersh, MD, Chase-Brexton Health Services, Baltimore, MD; Kevin Cranston, MDiv, MA Dept of Public Health, Boston, MA; Kathy McNamara, RN, NACHC, Bethesda, MD; Laura Cheever, MD, ScM, HRSA, Rockville, MD; William Tonkins, HRSA, Rockville, MD; Lyman Von Nostrand, MPA, HRSA, Rockville, MD; Susan Moskosky, MS, RNC, OPA, Washington, DC; Sarah Wattenberg, MSW, SAMHSA, Rockville, MD

Discordant Couples and Conception Expert Panel: Robert Maupin, MD, LSU, New Orleans, LA; Jean Anderson, MD, Johns Hopkins/ACOG, Baltimore, MD; Donna Sweet, MD, Kansas/ ACP, Wichita, Kansas; Ron Goldschmidt, MD, UCSF/AAFP, San Francisco, CA; Christine Lubinski, IDSA/HIVMA, Washington, DC; Kathleen Squires, MD, HIVMA, Arlington, VA; Arlene Bardaquez, MD, MPH, HIVMA, Arlington, VA; Michael Lindsay, MD, MPH, Emory/Society of Maternal-Fetal Medicine,

Atlanta, GA; Michelle Roland, MD, NASTAD, San Francisco, CA; Julie Womack, CNM, APRN, PhD, VAMC/Am Coll Nurse Midwifery, West Haven, CT; Pat Flynn, MD, MS, AAP, Memphis, Tennessee; Anonymous (HIV+ woman in discordant couple); Songhai Barclift, MD, HRSA, Rockville, MD; Karen Hench, RN, MS, HRSA, Rockville, MD; Heather Watts, MD, NICHD, Bethesda, MD; Kim Struble, PharmD, FDA, Silver Spring, MD; Linda Lewis, MD, FDA, Silver Spring, MD; David Thompson, SAMHSA, Rockville, MD; Susan Moskosky, MS, RNC, OPA, Washington, DC

Network Sciences Expert Panel: Alan Neaigus, PhD, Columbia/NYC DOH, New York, NY; Carl Latkin, PhD, JHU, Baltimore, MD; Irene Doherty, PhD, UNC, Chapel Hill, NC; Malcolm Steinberg, MD, MSc, CDC-Canada, Ontario, Canada; Mark Williams, PhD, UT SPH, Houston, TX; Martina Morris, PhD, MA, UW, Seattle, WA; Thomas Valente, PhD, USC, Alhambra, CA; Neil Abernethy, PhD, UW, Seattle, WA; Donna Smith, GSU, Atlanta, GA; Richard Rothenberg, MD, GSU, Atlanta, GA; Mark Mulligan, MD, Emory, Atlanta, GA

Public Health Law and Regulatory Issues Expert Panel: Larry Gostin, JD, Georgetown, Washington, DC; Shelley Hayes, JD, ABA, Washington, DC; Scott Burris, JD, Temple, Philadelphia, PA; Abigail English, JD, UNC, Chapel Hill, NC; Judith Waltz, JD, Foley & Lardner, San Francisco, CA; Kevin Cranston, MDiv, MA Dept. of Public Health, Boston, MA; Kim Struble, PharmD, FDA, Silver Spring, MD; Nan Feyler, JD, MPH, Office of the Philadelphia Commissioner of Health, Philadelphia, PA; Christopher Bates, MPA, OHAP, Washington, DC; Jesse Vivian, RPh, JD, Wayne State, Detroit, MI; Ryan Clary, Project Inform, San Francisco, CA; Jim Rooney, MD, Gilead Sciences, San Francisco, CA (observer).

Insurers and Benefits Managers Expert Panel: Sam Nussbaum, MD, Wellpoint, Indianapolis, IN; Ed Pezella, MD, MPH, Aetna, Hartford, CT; Amanda Charbonneau, Kaiser Permanente, San Francisco, CA; Paurvi Bhatt, MPH, Levi Strauss, Evanston, IL; Roger Snow, MD, MassHealth, Boston, MA; Charles Gonzalez, MD, NYS DOH, New York, NY; Justin Goforth, Whitman Walker, Washington, DC; Ann Donnelly, Project Inform, San Francisco, CA; Brian Bongner, NACCHO, Waukegan, IL; Ernest Hopkins, SF AIDS Foundation, San Francisco, CA; Tyler TerMeer, NASTAD, Washington, DC; Coy Stout, MSW, Gilead Sciences, San Francisco, CA (observer).

2014 External Peer Reviewers:

Kenneth Mayer, MD, Fenway Institute, Boston, MA; Susan Buchbinder, MD, SF DOPH, San Francisco, CA; Charles Gonzalez, MD, NYS DOH, New York, NY; Kimberly Y. Smith, MD, Rush University College of Medicine, Chicago, IL; Sylvia Amesty, MD, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, New York, NY; Michael A. Kolber, PhD, MD, University of Miami Miller School of Medicine, Miami, FL

2014 CDC NCHHSTP PrEP Working Group Members:

Dawn K. Smith, MD, MS, MPH, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP); Anita Alston, PhD (cd.), MBA, NCHHSTP; Gillian Anderson, MPH, Center for Global Health (CGH); Steve Nesheim, MD, NCHHSTP; Drew Voetsch, PhD, MPH, CGH; Linda Koenig,

PhD, NCHHSTP; Ann O’Leary, PhD, NCHHSTP; Marlene Glassman, PhD, MSW, NCHHSTP; Luke Shouse, MD, NCHHSTP; John Beltrami, MD, NCHHSTP; David Miller, BA, NCHHSTP; Susan Shewmaker, MA, NCHHSTP; Chezia Carraway, MSW, NCHHSTP; Paul Farnham, PhD, NCHHSTP; Laura McElroy, BA, NCHHSTP; Erin Connelly, MPA, Office of Noncommunicable Diseases, Injury, and Environmental Health (ONDIEH); Stan Lehman, MPH, NCHHSTP; Amy Lansky, PhD, MPH, NCHHSTP; Sam Dooley, MD, NCHHSTP; James Heffelfinger, MD, NCHHSTP; Joel Fletcher, BBA, NCHHSTP; Zinzi Bailey, MSPH, NCHHSTP; Jim Carey, PhD, NCHHSTP; Jeff Herbst, PhD, NCHHSTP

2014 Other CDC Scientists and Staff:

Salaam Semaan, DrPH, NCHHSTP; Eleanor McClellan, MA, NCHHSTP; Peter Kilmarx, MD, CGH; Paul Weidle, PharmD, MPH, NCHHSTP; Chris Cagle, PhD, NCHHSTP; Amitra Patel, MPH, NCHHSTP; Rebecca Morgan, MPH, NCHHSTP; David Purcell, JD, PhD, NCHHSTP; Eva Margolies, MPA, NCHHSTP; Terry Chorba, MD, MPH, DSc, NCHHSTP; Michelle Owens, PhD, ONDIEH; Dale Stratford, PhD, MA, NCHHSTP; Raul Romaguera, DMD, MPH, NCHHSTP; Jeff Bosshart, MSW, MPH, NCHHSTP; Stephanie Sansom, MPP, MPH, PhD, NCHHSTP; Maurizio Macaluso, MD, DrPH, NCCDPHP; Denise Jamieson, MD, MPH, ONDIEH; Margaret Lampe, BSN, MPH, NCHHSTP; Madeline Sutton, MD, NCHHSTP; Anthony Moulton, PhD, LSPPPO; Lindsay Culp, JD, MPH, OSTLTS; Stuart Berman, MD, NCHHSTP; Chesley Richards, MD, OADP; Lydia Ogden, MA, PhD, OADP.

Potential conflicts of interest:

CDC and individual employees involved in the guideline development process are named in US government patents and patent applications related to methods for HIV prophylaxis.

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Participants in 2021 Guidelines Update

Name (Affiliation)	Role	Potential Financial Competing Interest
Dawn K. Smith, MD, MS, MPH CDC	Lead Author, DHAP Writing Team	None
John T. Brooks, MD CDC	Member, DHAP Writing Team	None
Gema Dumitru, MD CDC	Member, DHAP Writing Team	None
Karen W. Hoover, MD	Member, DHAP Writing Team	None

CDC		
John Weiser, MD CDC	Member, DHAP Writing Team	None
Luke Shouse, MD CDC	Member, DHAP Writing Team	None
Elliot Raizes, MD	Member, DHAP Writing Team	None
Douglas Krakower, MD	Nonfederal External Reviewer	None
Jonathan Iralu, MD	Nonfederal External Reviewer	None
Katherine Frasca, MD	Nonfederal External Reviewer	None
Jenell Coleman, MD, MPH	Nonfederal External Reviewer	None

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 foundation 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.

SYSTEMATIC LITERATURE REVIEW METHODS

For the 2014 guidelines, a systematic review was conducted of PrEP studies published from January 2010 through December 2013. For the 2017 guidelines, the same search strategy was run to update studies published through June 2017. For the 2021 guideline, Descovy and cabotegravir were added to the search strategy and studies published through December 2020 were identified. Searches were conducted of MEDLINE, Embase, CINAHL, and Cochrane Library databases. The 2021 search strategy used the following criteria:

- Pre-Exposure Prophylaxis/ OR Chemoprevention/ OR (((Preexposure OR Pre-exposure) adjacent to prophylaxis) OR PrEP OR (topical adjacent to (prevention OR prophylaxis OR microbicide* OR gel OR pericoital OR precoital OR vaginal OR rectal OR anal)) OR chemoprophylaxis OR chemoprevention OR chemo-prophylaxis OR chemo-prevention OR iPrEX).mp.
- AND
- (exploded terms) Anti-HIV Agents/ OR Anti-Retroviral Agents/ OR HIV Infections/pc OR ((HIV OR human immunodeficiency virus) AND (antiretroviral* OR anti-retroviral*

OR antiretrovirus* OR anti-retrovirus* OR Truvada OR tenofovir OR emtricitabine OR (TDF ADJ5 FTC) OR Descovy OR cabotegravir))

- AND NOT animals
- in the title, abstract, keyword heading word, subject heading fields

Retrieved citations were provided in an Endnote reference file for deduplication. Then 2 scientists independently reviewed the citations and removed articles that were not published in English, did not contain data (e.g., editorials, reviews, news reports), or did not contain data about oral TDF/FTC or cabotegravir injections for PrEP. The next step was to screen citations to remove articles that did not contain new data about oral PrEP (data/analyses not previously published). For the 2021 update, year of publication, author, and titles were compared with the 2017 Endnote library as necessary to identify already existing entries. During this step, abstracts or full articles were read and publications were categorized into the following groups:

- New clinical trial results;
- New human observational study results;
- New survey, focus group, or other behavioral study results;
- New cost analysis results (e.g., program cost, cost benefit analysis);
- New modeling results (e.g., impact models);
- New laboratory human study results (e.g., drug levels, resistance); or
- None of the above.

The coding by the two reviewers was then compared and discrepancies were reconciled. Citations with no new data about daily oral PrEP with TDF/FTC or cabotegravir injections were deleted from the updated Endnote 2020 library.

Data from the clinical trial, human observational study, and laboratory human study results were added to the evidence tables. Study findings presented in the evidence tables were each assessed for quality of the study using GRADE criteria¹⁸ (see guidelines Appendix 1, Table 8). Then all data supporting a specific recommendation were given a summary strength of evidence rating (across all studies relevant to that recommendation) using the same system as used for the DHHS antiretroviral treatment guidelines¹⁷ (see PrEP clinical practice guidelines Appendix 1, Table 9).

DRAFT GUIDELINE WRITING AND REVIEW PRIOR TO PUBLICATION

The draft was written to address guidelines standards for review of the strength of evidence (GRADE approach¹⁸) as well as a format designed to promote guideline implementation (GLIA¹⁹), dissemination (GEM²⁰), and adoption (AGREE²¹).

The 2014 draft clinical practice guideline and clinical 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.

For the 2021 update, the systematic review of published literature was updated through December 2020, additions to the evidence review tables were made; minor clarifying edits to the supporting text were made to enhance consistency with recently updated STD, nPEP, and perinatal guidelines sections relevant to PrEP; and updated references were added. For the 2021 update, changes to the graded recommendations were made to include adolescents, Descovy, and cabotegravir for PrEP (see “What’s New” page in the 2021 guidelines). The updated guideline was then shared with a group of 4 external peer reviewers for comment and public comment on the changes was obtained.

[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 use, 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 for PrEP.

When significant new data become available that may affect patient safety or graded recommendations for PrEP use, an announcement with suggested revisions to the existing guidelines will be posted on the CDC web site for a 2-week public comment period. These comments will be reviewed and a determination made as to whether additional revisions to the guideline are indicated. Final updated guidelines will then be posted on the CDC web site.

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