A publication for medical and non-medial service providers

PRE-EXPOSURE PROPHYLAXIS

Talking to patients about Pre-Exposure Prophylaxis

your life matters

PROJECT INFORM

OCTOBER 2013

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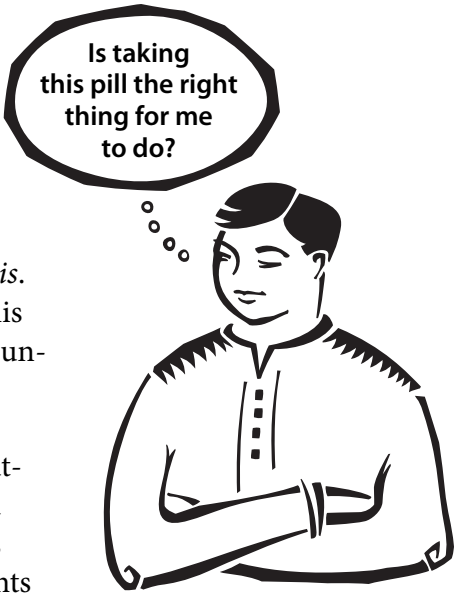
Using this booklet ...



Project Inform wrote this publication for health care workers who interact with people who may have questions about PrEP, or *Pre-Exposure Prophylaxis*. Project Inform provides this information to help test counselors, outreach workers, nurses, medical and non-medical case managers, outpatient administrators and others to answer questions that your clients and patients may have about PrEP.

Two other Project Inform publications, *Is taking PrEP the right choice for you?* (one for men and transgender women who have sex with men and one for heterosexual men and women), are also available for your patients or clients to read. They can be accessed at *www.projectinform.org/prep*.

Additionally, Project Inform developed four educational videos on PrEP for men who have sex with men. They can be viewed at the previous URL and also at *vimeo.com/prepvideos*.

Quick facts about PrEP ...

- PrEP works if you take it. People who take PrEP as prescribed (daily) may have up to 99% protection when other prevention methods are also used.
- PrEP is a single pill called Truvada that contains two anti-HIV drugs and is taken once daily to prevent HIV infection in people who are at high risk for it.
- PrEP is recommended along with other prevention methods, such as using condoms.
- PrEP must be used with the support of a health care provider. However, since PrEP was just recently approved by the FDA, some doctors may not know about it or may not be willing to discuss PrEP with their patients.
- Taking PrEP includes getting routine blood tests done.
- PrEP may cause side effects.

What is PrEP, and how is it different from PEP?

PrEP means that a person takes a drug before they are exposed to a virus or bacteria to prevent becoming infected. In this case, an HIV-negative person would take the pill called Truvada to prevent HIV infection.

Two studies show that HIV-negative people who are able to take Truvada for PrEP every day or nearly every day — and who combine it with condoms and other HIV prevention methods — may see their HIV risk cut by up to 99%. This is true in both women and men and for both vaginal and anal sex. Based on these studies, the US Food and Drug Administration (FDA) approved Truvada for PrEP in July 2012 for adults at high risk for sexual transmission of HIV.

PrEP is not just about taking a pill every day. Individuals who decide to take PrEP will need to see their doctors at least every three months for routine care and testing. They'll need to talk about their current sexual activity, their level of risk, STDs, routine test results and any side effects. This means more doctor visits, refills, co-pays, and extra attention to an overall HIV prevention strategy for people who decide to use PrEP.

On the other hand, *Post-Exposure Prophylaxis* or PEP, involves taking medicines after a person is exposed to a virus or bacteria. In this situation, a person would usually take several medications for about one month after a high-risk exposure to HIV.

Who are good candidates for PrEP?

The FDA states that Truvada "is indicated, 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" for becoming infected. This is a broad indication that covers several groups of individuals.

Below is a list of questions you may ask your patients or clients. If they answer "yes" to any of them, they might be a good candidate for PrEP and should be evaluated by a health care provider.

- Is your primary sexual partner HIV-positive? In other words, are you part of a mixed-status couple?
- Has a man — particularly an HIV-positive man or a man whose status you aren't sure about — penetrated you during vaginal or anal sex without a condom recently?
- Have you been treated recently for a sexually transmitted disease in your vagina or butt, such as gonorrhea?
- Have you used PEP more than once within the past year?
- Have you been in prison; or, has your sex partner(s)?
- Do you use drugs and alcohol heavily; or, does your sex partner(s)?
- Do you have to exchange sex for money, housing or other needs; or, does your sex partner(s)?
- Has your partner threatened you with violence or physically harmed you recently?
- Are you in a mixed status relationship and one of you is trying to have a baby?

Not everyone who engages in the behaviors described above should necessarily go on PrEP. Some people, with counseling and support, may be able to adopt other risk reduction behaviors to protect themselves. However, for some people PrEP may be an excellent HIV prevention option.

Who are not good candidates for PrEP?

A person ***should not use*** PrEP if they:

- Don't know their HIV status.
- Are HIV-positive (Truvada is not a complete regimen for people with HIV).
- Recently engaged in high risk HIV behaviors and have symptoms of acute HIV infection (similar to the flu).
- Can't locate a health care provider to provide regular HIV and STD testing and prevention counseling along with the medication.
- Don't think they can take the pill on time every day or nearly every day.
- Don't know whether they have hepatitis B.
- Want to "disco" dose their PrEP, or just take it from time to time such as over a weekend of partying.
- Have existing kidney disease or kidney dysfunction (Truvada may worsen kidney health).

What is Truvada and how does it work?

Truvada is a single tablet made up of two HIV medications — Viread (tenofovir disoproxil fumarate) and Emtriva (emtricitabine). Truvada has only been used until now with other HIV meds to treat HIV infection. Viread is also used to treat hepatitis B.

Truvada prevents HIV from reproducing in the body. If an HIV-negative person is exposed to the semen, pre-cum or vaginal fluids from an HIV-positive person, then Truvada can help to keep the virus from causing a lasting infection.

What are Truvada's side effects?

Because the majority of people in the completed PrEP studies were on the drugs for less than two years, only the shorter-term side effects for HIV-negative people are known at this time. The true long-term side effects, if any and if different from those experienced by HIV-positive people on treatment, are unknown at this time.

The very short-term side effects included headaches, weight loss and gastrointestinal problems like nausea, diarrhea and abdominal pain. These typically resolved in the first few weeks after starting Truvada. Some people also experienced minor reductions in their bone and kidney health, which were reversible when Truvada was withdrawn.

However, in HIV-positive people, Truvada can cause lasting bone loss and can damage the kidneys over time in a minority of those who take it. Because HIV by itself can also cause these same problems, it is difficult to determine how much Truvada alone contributes to kidney and bone disease.

At a minimum, HIV-negative people with current kidney dysfunction (a *creatinine clearance* <60 mL/minute) should not use PrEP. Those who do use PrEP should be regularly monitored for changes in their kidney and bone health.

How well does Truvada prevent HIV infection?

What we have learned, essentially, is that PrEP works if you take it. In clinical studies, when people took Truvada as close to every day as possible, the pill appeared to lower their risk for infection by up to 99%. Success was lower in people who took it less often, which makes sense. Medications can't work if they aren't taken properly. PrEP is no different, which is why adherence support will be critical to ensuring that PrEP is used with the highest degree of effectiveness.

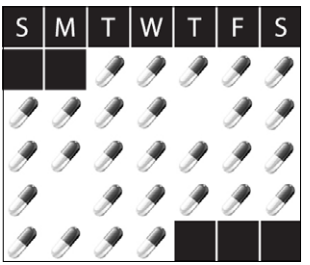
When the FDA reviewed the available data on Truvada for PrEP in order to decide whether to approve it for this purpose, most of the evidence they considered came from two large clinical studies.

One of them, called iPrEx, was conducted in 2,499 high-risk gay men and other men who have sex with men, and a small number of transgender women who had sex with male partners. The international study had sites in the United States, Peru, Equador, Brazil, Thailand and South Africa. Individuals were at fairly high risk for HIV when they entered the study. Most stated having unprotected receptive anal intercourse in the previous several months and many had had an STD.

The iPrEx participants were randomized to receive either Truvada or a placebo, along with HIV risk reduction counseling, condoms and adherence support for all. During the study a small group of those who were assigned to take Truvada were randomly selected to have the levels of the two drugs in Truvada measured inside their blood cells where the drugs are active. This is a more effective way to measure a person's adherence than simply measuring whether the drug is present in blood. This is because cellular levels of the drug take longer to build up and go away, so you can more closely estimate how many doses a person was recently taking.

How well does Truvada prevent HIV infection?, *continued*

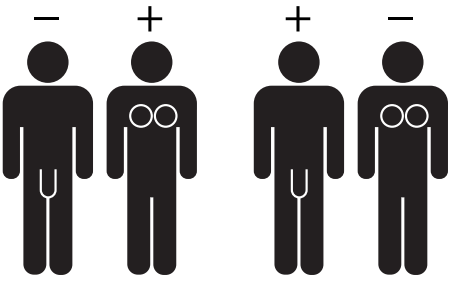
When the iPrEx researchers compared HIV infection rates in all of those assigned to take Truvada — whether or not they actually did — the risk of infection was 42% lower than in those who had taken a placebo. Though the participants stated that they'd been taking most of their doses, the cellular drug levels told a different story. In fact, less than half of those in whom drug levels were tested actually had detectable drug.



This led the researchers to look at the degree of efficacy only in those whom drug levels were high enough to indicate daily, or near daily, dosing.

In this group, they found that HIV transmission rates were cut by at least 90%. What's even more encouraging is that when the researchers compared the infection rate based on the participant's Truvada blood levels with the Truvada blood levels of another group of people taking PrEP either two days per week, four days per week or every day, they found that daily use resulted in 99% efficacy. A four-dose-per-week strategy reduced infections by 96% and even those who were estimated to have taken PrEP only twice per week had over 70% efficacy. These findings have two implications. The first is that when taken properly, Truvada has a very high degree of efficacy. The second, more sober finding, is that people may have significant challenges with adherence (which they may not disclose), and that they may need specially designed forms of support both to assess their daily adherence and to help overcome any obstacles.

How well does Truvada prevent HIV infection?, *continued*



The second large study was quite different in some regards from iPrEx. That study, Partners PrEP, was conducted in 4,758 heterosexual couples where one partner was HIV-positive and the other HIV-negative, or what are commonly referred to as either *sero-discordant* or *mixed-status* couples. All participants were recruited in either Kenya or Uganda.

Partners PrEP also compared Truvada to a placebo, but it had a third arm as well where people were assigned to take the single drug Viread. Though Viread performed statistically similar to Truvada in this study, it is not being pursued actively for PrEP at this time. Therefore, results are not reported here.

Overall, the Partners PrEP researchers found that those assigned to take Truvada were 75% less likely to become infected with HIV. Truvada offered equal levels of protection to men and women. As with iPrEx, the Partners PrEP researchers looked at drug levels, but they tested blood rather than cellular concentrations. They found exactly the same results, however. Those with substantial levels of Truvada in their blood had their HIV risk slashed by 90%. A recent analysis of those with perfect or near-perfect adherence to PrEP found a reduction in HIV risk of 99%.

However, the results of two other studies raised some concern about the efficacy of Truvada in women. In one study, called FEM-PrEP, young HIV-negative women in Kenya, Tanzania and South Africa took either Truvada or a placebo.

How well does Truvada prevent HIV infection?, *continued*

However, FEM-PrEP was stopped early because there was no difference in effectiveness between the two groups. However, a later analysis found that almost 75% of the women were not taking their pills, which likely affected the results of the study. This newer analysis helped address concerns that Truvada might work less well in women. What also became clear was that accurate risk assessments and communications of risk assessments will be critical to PrEP among other prevention tools. The women in FEM-PrEP felt themselves to be at low risk of becoming infected, even though their actual risk was very high. This may have caused them to be less motivated to take their medication.

Another study, called VOICE, had essentially the same result as FEM-PrEP. In VOICE, women were randomized to receive a placebo pill, a placebo vaginal gel, a tenofovir gel, a tenofovir (Viread) pill or Truvada. None of the three arms of the study found that these interventions worked, and as with FEM-PrEP it is almost certain that this was due to very low adherence to the gel and pills.

Given the high degree of effectiveness in the Partners PrEP study, however, there is good reason to believe that PrEP can be quite effective for women if they can take it regularly.

Will taking Truvada as PrEP lead to drug resistance?

When people take too little of a drug or take it too infrequently, this can allow HIV to mutate and develop resistance to those drugs, rendering them ineffective. Because Truvada is an incomplete HIV regimen, there was initially some concern that people who became infected while taking PrEP might develop resistance to one or both of the drugs in Truvada.

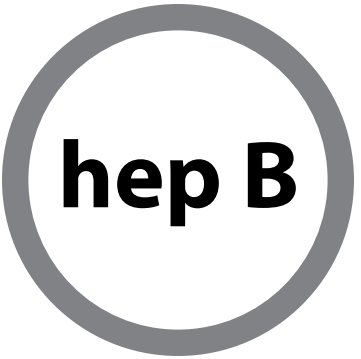
So far, however, not a single person who was confirmed to be HIV-negative at the time they started PrEP has developed drug resistance after becoming infected. This was true in all five studies and even in people who had low levels of Truvada in their blood at the time they tested HIV-positive in the study.

A few people did develop drug resistance, but these individuals were all later confirmed to have been HIV-infected at the time they started taking PrEP. They just happened to be in acute infection, which means they were infected so recently that they didn't yet have enough HIV antibodies to test positive on an antibody test.

What about drug interactions?

Because PrEP could be prescribed to men and women over a range of ages, it's important for people to review possible drug interactions with other medications and other-the-counter products they take. Examples include birth control pills, hormonal pills, testosterone, heart medicine, diabetes medicine, etc.

Why is it important to test for hepatitis B before start PrEP?



Both of the drugs in Truvada are active against hepatitis B, as well as HIV. Therefore, it's important for individuals to know if they have hepatitis B before they start PrEP.

For some people with active hepatitis B, taking Truvada (Viread+Emtriva) may be inadequate at controlling the virus and could eventually cause drug resistance to occur. Further, stopping these drugs during undiagnosed hep B disease can cause a spike in its replication, which can result in a dangerous inflammatory condition in the liver called a flare.

Before a person starts PrEP, they should be tested for active hepatitis B disease. If the results show they don't have it and haven't been exposed to it, then they should be encouraged to get a hep B vaccination series to prevent the infection while they're on PrEP. If the results show they were exposed earlier to hepatitis B and the infection has resolved, then they can't get hep B again. However, if the results show they have active disease, then a medical provider should assess their liver health and hepatitis B status for a treatment regimen if warranted.

It is possible for individuals with hep B to take PrEP. However, they should work closely with their medical providers on the safest way to start and stop PrEP in this situation.

How important is adherence?

As detailed on pages 8–10, *How well does Truvada prevent HIV infection?*, adherence is critically important to ensure the highest level of protection against HIV. Not taking PrEP every day or nearly every day can increase a person's risk.

Since adherence is critical, individuals may need additional adherence support from their medical and non-medical providers. This would include brainstorming ideas to improve adherence. Some areas to discuss with your patients and clients include practical support (cell phone alarms, refilling prescription, regular doctor visits, etc.), scheduling support (where they'll take it, best time to take it, addressing irregular schedules, etc.), and psycho-emotional support (address depression, assess alcohol and drug use, etc.).

Some people find it fairly easy to take pills every day, like taking a daily vitamin. This can be easier if taking the dose happens at the same time that a routine activity occurs, like shaving or eating breakfast or brushing teeth before going to sleep.

It can also help if the pill bottle is in plain view as a reminder like on a night stand or bathroom shelf. Many people use gadgets like a cell phone alarm, or services that offer text message and email reminders. Many of these methods may only have to be temporary support until they get into the habit of taking their pill.

How long is PrEP used for?

In a nutshell, it depends upon the individual. People should use PrEP over that period of time when they are at high risk for getting HIV. Some people may use PrEP for only a few months, perhaps as a result of a relationship breaking up. Others may find the need to take it over years, as they may struggle with finding alternative risk reduction activities that work for them while addressing other issues such as alcohol use.

Still others may want to start for awhile, stop for some time, and then re-start for another period of time. Making this type of decision — when to use PrEP as well as when not to use it — should be done with help from your patient's or client's health care provider.

When is PrEP stopped?

If your patient or client finds out that they've become infected with HIV, they should immediately contact their health care provider. Taking an inferior HIV regimen (Truvada is only part of a full HIV regimen) can result in the virus becoming resistant to the drugs in Truvada. If that happens, the individual won't be able to take Truvada as part of their future regimens, which could severely limit their treatment options over time.

Other reasons to stop PrEP include: trouble with side effects, changes in the level of HIV risk, adherence issues, or simply wanting to stop. In each of these cases, it's important to talk to your patient or client before they stop PrEP to make sure they're engaging in other activities that lower their risk of HIV.

Again, it's important to note that stopping PrEP when someone has hepatitis B can cause severe liver inflammation. In this case, stopping should be done with their doctor's help and monitoring.

What tests are needed before and during PrEP?

Before PrEP is started, the following tests and exams should be done by a health care provider:

- A thorough discussion about the patient's sexual activity and level of HIV risk
- An HIV antibody test and possibly an HIV RNA test
- Tests for hepatitis B, kidney function and STDs

While PrEP is used, the following should be done:

- Regular doctor visits every 2 to 3 months to assess blood work, side effects, adherence and risky activity.
- Routine HIV antibody tests (at least once every 3 months) to ensure continued HIV-negative status.
- STD tests done every 6 months, or more often if risk for STDs stays high.

How can PrEP be provided when we want people to use condoms?

Condoms are great. They are the cheapest and easiest way to avoid getting infected with HIV (aside from abstaining from high-risk activities). However, PrEP is a reasonable option for some people, especially if regular condom use is a struggle, as it could be one of the best ways to prevent people from getting infected while they work on the issues that keep them from using condoms or adopting other prevention methods.

A significant concern is that taking PrEP will lead to something called *risk compensation*. This means that if you think you are protected in one way, you take more risks in another. This would be similar to driving more recklessly because you are wearing a seat belt or have air bags in your car.

How can PrEP be provided when we want people to use condoms?, *continued*

Experts have grown at least somewhat less concerned about this for several reasons. First, risk actually went down in every study conducted so far. This is probably because people were counseled regularly on safer sex and given free condoms. Second, people who are good candidates for PrEP are people who already struggle a great deal with condom use. PrEP is not for people who use condoms every time or nearly every time.

It should be noted that some people, particularly women, trans-women and gay men (and other MSM) are at significantly increased risk from partner violence and have partners who refuse to use condoms. Until other prevention methods become available, PrEP is the only prevention tool that is within the control of the person who wishes to protect her or himself and doesn't require the cooperation of a sex partner.

What community advocates, public officials, health care providers and others are trying to understand is how to target PrEP most appropriately now that we know that it actually works (and works very well when taken properly). If a person almost always uses condoms, PrEP is probably not the most appropriate prevention intervention. For a person who rarely if ever uses condoms for receptive anal or vaginal sex then PrEP could be an ideal option.

People give a variety of reasons for not using condoms. These include, but are not limited to:

- An inability of some people to insist that their partner(s) use one
- The reality that condoms affect physical sensation during sex

How can PrEP be provided when we want people to use condoms?, *continued*

- The reality that some people feel that condoms imply a lack of trust or love between them and their partner(s) and that not using them increases a feeling of love and intimacy
- The reality that some people who are depressed or who use drugs and alcohol heavily have difficulty using condoms appropriately
- The reality that some people believe that their partner(s) have little chance of being HIV-positive when in fact that chance is remarkably high, particularly true in communities of color in some parts of the United States.

Ideally, people will increase their condom use while taking Truvada for PrEP (as seen in iPrEx and Partners PrEP) and they should be supported in that behavior. This may be possible for some, but unlikely for others. If we are to be ultimately effective in our shared goal of lowering the number of new HIV infections among the people we serve, then we must find ways to work with both types of individuals and to realize that PrEP combined with few or no condoms is still much better than nothing combined with few or no condoms.

Demonstration projects — which follow how scientists and public health officials roll out a new intervention like PrEP in the real world — may help us answer some of these critical questions. Projects are either ongoing or planned in multiple countries and involving nearly 20,000 people. The first demonstration projects will begin reporting results in the next couple of years. In the meantime, we will have to use everything we have learned from nearly 30 years of HIV prevention research to adequately identify those who will be the best candidates for PrEP and to identify the tools most suited to helping them stay HIV-negative — including PrEP.

What if a person becomes infected with HIV while taking PrEP?

In this case, there are two issues: inadequate HIV treatment and drug resistance. Since HIV-positive people take three or more medications to control their infection, only taking the two drugs in Truvada would be insufficient to adequately control the virus over time. They should contact their provider immediately should they find out their status from another source.

When inadequate levels of HIV meds are used, new strains of the virus can develop that avoid the effects of the drugs. This drug resistance allows HIV to reproduce despite the presence of the drugs, and eventually make the drugs useless. Since Truvada is prescribed in most HIV regimens, not being able to use it due to resistance issues could limit an individual's treatment options over time.

Two things can be done to help prevent drug resistance:

- ***Before starting PrEP***, ensure the patient is HIV-negative. Although antibody tests help establish a person's status with a high level of reliability, it's only as good as the window period for initial HIV infection. Should a patient have recent high-risk activity after an earlier negative antibody result but before they start PrEP, they could still be infected. In this case, it may be wise for them to wait to get another test later and start PrEP based on the second result or to have an HIV RNA test conducted. In a small number of people in PrEP studies, the person was actually infected, but hadn't produced enough antibodies to test positive. In some of these cases, the person went on to develop drug resistance to the components of Truvada.
- ***While on PrEP***, ensure the patient gets routinely tested for HIV every 3 months. Individuals should tell their provider if they develop flu-like symptoms or unexplained rashes in between HIV tests.

Where do you get PrEP and how much will it cost?

Since PrEP is approved by the FDA, individuals should hopefully be able to get the prescription covered by their health insurance if they have it. It should also, hopefully, be available through government insurance programs such as Medicaid. Because PrEP is an entirely new HIV prevention strategy, not all insurance companies or state insurance programs have decided whether to cover PrEP yet. It is possible that some may choose not to pay for it.

For people whose insurance does cover PrEP, the major cost should only be the drug co-pay charged at the pharmacy and co-pays for doctor visits and lab tests. Gilead Sciences, which makes Truvada, will cover the co-pays for the drugs. In order to access that program, go to *www.truvada.com* or call 888-358-0398. Because of the rules associated with public insurance programs, Gilead cannot cover co-pays for Medicaid or Medicare or for people residing in Massachusetts.

For people without insurance, or whose insurance won't cover PrEP, Gilead has agreed to offer help to those with lower incomes. To learn more about this program, go to *https://start.truvada.com*.

Gilead has also agreed to provide vouchers for free HIV tests and free condoms for those taking PrEP. Information about free HIV testing and condoms can also be found at *https://start.truvada.com*.

If your patient or client is interested in PrEP, but doesn't have a provider with whom they can discuss it, they could contact their local health department's HIV or STD program. They may know about local PrEP demonstration projects and may also be aware of clinics or hospitals offering PrEP services. You can also check Project Inform's website (*www.projectinform.org/prep/*) for links to demonstration projects and other information and videos about PrEP.

Other resources that may help

INFORMATION ON PrEP

Pre-Exposure Prophylaxis
www.projectinform.org/prep/

My PrEP Experience
http://myprepexperience.blogspot.com/

PrEP Facts
http://prepfacts.org/

Truvada for PrEP
(company website)
http://start.truvada.com/#

Truvada for PrEP
(company REMS website)
https://www.truvadapreprems.com/#

ARTICLES

The Math and Morality of PrEP
www.frontiersla.com/Blog/PositiveFrontiers/blogentry.aspx?BlogEntryID=10474103

Ask a Guinea Pig: What Do I Need to Know Before Joining a PrEP Trial?
http://betablog.org/ask-a-guinea-pig-what-do-i-need-to-know-before-joining-a-prep-trial/

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men
(clinical study data)
www.nejm.org/doi/pdf/10.1056/NEJMoa1011205

APPLICATION FORM

Medication Assistance Program
(for uninsured people to cover the cost of Truvada, work with doctor to fill it out)
https://start.truvada.com/Content/pdf/Medication_Assistance_Program.pdf

WEBSITES FOR CLINICIANS

Truvada for a PrEP Indication
https://start.truvada.com/

Clinical Studies Resources
www.avac.org/ht/d/sp/i/262/pid/262

CDC Fact Sheet (PrEP: A New Tool for HIV Prevention)
www.cdc.gov/hiv/prep/pdf/PrEPfactsheet.pdf

CDC Interim Guidance on HIV PrEP for Men Who Have Sex with Men
www.cdc.gov/nchhstp/newsroom/images/CDC-Interim-PrEP-Guidance.jpg

Interim Guidance for Clinicians Considering the Use of PrEP for the Prevention of HIV Infection in Heterosexually Active Adults
www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a2.htm?s_cid=mm6131a2_w

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