WEBINAR VIDEO TRANSCRIPT

Partnership for Care HIV TAC

Practical Strategies for Implementing PrEP in a Primary Care Setting

30 September 2015

MODERATOR: Good afternoon and welcome to the Practical Strategies for Implementing PrEP in a Primary Care Setting webinar. This webinar is brought to you by the Partnerships for Care HIV Training, Technical Assistance, and Collaboration Center, or HIV TAC. The Partnership's for Care project is a three-year multi-agency project funded by the secretary's Minority AIDS Initiative fund and the Affordable Care Act.

The goals of the project are to, one, expand prevention of HIV testing, prevention care, and treatment and help centers serving communities highly impacted by HIV. Two, build sustainable partnerships between health centers and their state health department. And three, improve health outcomes among people living with HIV, especially among racial ethnic minorities. This project is supported by the HIV Training, Technical Assistance, and Collaboration Center, HIV TAC.

Today's webinar will be led by Doctor Jeffrey Klausner. Doctor Klausner is a professor of Medicine and Public Health in the division of infectious diseases at UCLA Schools of Medicine and Public Health. Doctor Klausner earned his medical degree from Cornell University Medical College. He completed his residency in internal medicine at the New York University Bellevue Hospital Center.

Doctor Klausner earned his master's in public health at Harvard University with a focus on international health and epidemiology. Following that degree, Doctor Klausner was an epidemic intelligence service officer at the Centers for Disease Control and Prevention. Doctor Klausner completed his clinical fellowship in infectious diseases at the University of Washington- Seattle under the mentorship of professor King Holmes.

Please join me in welcoming Doctor Klausner.

DR. JEFFREY KLAUSNER: Good afternoon. Thank you. Well, welcome everyone to today's webinar on pre-exposure prophylaxis or PrEP, for HIV infection.

Today, September 30, 2015, is actually a momentous day for pre-exposure prophylaxis. The WHO released today its expedited guidelines on recommendations for making pre-exposure prophylaxis for HIV infection throughout the world. And this is really an important event today.

And along with those guidelines came recommendations from WHO that persons with HIV infection should be initiated on antiretroviral therapy, regardless of CD4 count. So all the policies were released today by the WHO.

So in a disclosure, I'm a faculty member at the University of California. I'm a guest researcher with the US CDC Mycotics, or fungal diseases, Branch. I'm a member the WHO STD guidelines group. I'm a board member of New Technology in Health a nonprofit, and an unpaid medical advisor for healthvana.com. For the type of work I do, which is research in HIV prevention, I receive funding from a variety of different public and private institutions.

So what we're going to do today, the goal is really to increase the capacity of your ability to provide Truvada for PrEP in a primary care setting. So we're going to increase your knowledge about the effectiveness and safety of Truvada for PrEP, enhance your capacity to identify those who would benefit from Truvada for PrEP, and understand when to prescribe Truvada for PrEP, and manage drug and behavioral side effects.

In order to meet those objectives, we're going to go through this outline talking about what is PrEP, how well does it work, is it safe, offering prep. Throughout the presentation, there are different cases that we will review and also entertain some questions about those cases. And then we'll share with you a variety of different resources that are available online. And also part of the handouts, there's two important resources for posters or pamphlets that people may want to use in their clinical setting.

So what is PrEP? So PrEP stands for pre-exposure prophylaxis and pre-exposure prophylaxis could be used for a variety of different conditions. In the context today, we're talking about pre-exposure prophylaxis, or PrEP, for HIV infection.

The only recommended treatment in the United States currently is the medication call Truvana, which is a combination pill of two antiretroviral medications, emtricitabine and tenofovir. It's used one pill once a day and it was actually FDA approved for use for the prevention of the acquisition of HIV infection more than three years ago in July 2012.

So the first polling question for the audience is how well does Truvada work for PrEP to prevent HIV? Please select one.

OK so we can see that there is a range of responses. The most common response was it depends. The second was 85%. Two people said 100%, and no one responded 65%.

So the next slide shows the effectiveness of Truvada in a variety of different clinical trials that have been done across the world. And you can see that the effectiveness of Truvada depends. It depends on the population in which it was studied. And further analysis of these studies really showed that it depended on adherence.

So the iPrEX trial, which was the first trial done in North and South America among men who had sex with men, actually showed an overall effectiveness of 42%. Some studies have been revised to show 44%, but that was clearly driven by adherence. When they looked at the population who had measurable drug in their bloodstream, the efficacy was actually 92%.

In the FEM-PrEP trial, which was a trial done in Africa, adherence was very poor. And you can see that the effectiveness was low.

In the CDC-support supported TDF2 trials, you can see that the effectiveness varied. Again, that was driven by adherence.

In the VOICE trial, which was another trial in Africa, there was actually no measurable effectiveness and adherence was extremely low.

The Partners PrEP trial, which was done in discordant couples-- and highlight that trial because that's an important target population in terms of people who would benefit from Truvada for PrEP are in discordant partnerships where one partner is HIV infected and the other is uninfected. And you can see, again, both for tenofovir only or tenofovir in combination with emtricitabine was between about a 60%-84% effectiveness.

More recently, there's been two trials, one in the United Kingdom and one in France, that show about an 86% effectiveness. And that's probably where we get about the 85% overall effectiveness measure from. But it's important that, when people do take the medication every day, the effect has been shown to be at least about 92% percent.

And I want to highlight this iPERGAY study. This one's a little bit different in terms of the methodology than the other studies. So in the iPERGAY study, which was done in France, PrEP was used on demand. So participants were instructed to take two pills anywhere two to 24 hours prior to sex, one pill 24 hours after, and then a third dose of one pill 48 hours after that. So essentially two pills before, one 24 hours after. one 48 hours after.

And in this study they saw an 86% reduction in the incidence of HIV. And this is called On Demand PrEP. On average, participants took about 14 doses a month. So they actually were taking a fair amount of PrEP over the course of a month. The CDC in US recommendations are still to use PrEP on a daily basis, but this study just provides some evidence that there may be alternative ways to use PrEP, particularly in populations that may not have regular, ongoing risk exposure.

So if someone's exposure is more episodic, it might be reasonable to use it in this alternative fashion, although this is not an FDA approved indication. The FDA approved indication is to use it on a daily basis. And for many people, and particularly in my practice, daily therapy is just easier for people to comply with. In my practice, I currently have people who may not be at highest risk in terms of exposures on a regular basis, but they prefer to take it on a regular daily basis.

So polling question number two. What are some common side effects of Truvada for PrEP to prevent HIV?

OK so their responses are in. It's about relatively evenly split. A little bit more people responded that mild nausea and weight loss was the most common. Some other people said skin rash or fever, some vomiting. A couple said cardiac arrhythmia. And no one said any birth defects, particularly if used in the first trimester.

So our next slide, the safety of Truvada, really is a summary from the clinical trials. The most common would be mild, short-term nausea or diarrhea, some decreased appetite, and weight loss. So it's really mild nausea and weight loss, or answer B would be the correct response. There's really no significant increase in rashes, fever, or vomiting.

Over time, there have been some reversible small decreases in bone density. But those are identified. They are reversible and no increase in any bone fracture that one might expect if they were substantial decreases in bone density. And then, additionally, reversible small decreases in kidney function, such as creatinine clearance. So in a few individuals in the study, they had a small bump in their creatinine that, again, was reversible upon discontinuation.

In the women who received Truvada or tenofovir there were no increases in birth defects. So again it's felt it is generally safe in pregnancy, but it's important to weigh the risks and benefits of its use in pregnancy. And there were no serious adverse events in terms of cardiac or liver toxicity.

On the behavioral or sexual health side, it's been fairly consistent that studies the US and Europe have shown, among Truvada users for PrEP, that there has been a decrease in report condom use. And because the recommendations include frequent STD testing at baseline and follow up, there has been well-documented high rates of syphilis and rectal gonorrhea and chlamydia.

However we don't really know if we're increasingly identifying those because we're doing more testing or there's a true incidence of infection. And that's why it is important that, as part of prescribing PrEP, that there are available routine STD screen services and some risk reduction counseling and promotion of condoms, which we'll get into a little bit later.

So the key steps in a program, and as people are thinking about implementing PrEP for HIV in their own clinical settings, it's important to think about does your clinic population see populations at risk. And those are the young men who have sex with men, men who have sex with men of color, men who have sex with men in general, those attending STD clinics. So you might be in primary care setting. People may go elsewhere for STD care, but may come and see you for their primary care. Other risk groups include sex workers and sex partners of injection drug users.

And that's really, kind of, the key aspect of what we need to do. We need to identify those patients at risk. And I spend several slides coming up in terms of how to identify people at risk because we cannot provide the benefit of this prophylaxis if we don't know our patients and know our risk population.

This actually is to identify the clinical setting. Primary care seems a very appropriate setting to be offering people prophylaxis to prevent serious medical consequences, infection, something like HIV. While HIV is generally treatable, it's still highly stigmatized. It's still costly and there's still toxicity associated with long-term use of a highly active antiretroviral therapy. So it's important and worthwhile to prevent.

The cost, this requires different aspects of prescribing and management and follow up. It's recommended that people train different workers in their setting, that there'd be a medical provider, a social worker, phlebotomist. They need to be included as we think about what kind of blood tests should be obtained on a routine basis and other health workers.

I helped set up the AIDS Project Los Angeles Baldwin Hills primary care program for PrEP. And one of the first key steps was to just develop some simple written protocols in terms of who should be offered PrEP, who should not be offered PrEP, what the follow-up schedule should look like, and what testing should be included at each visit.

It's important, in your settings, to have educational and outreach tools. I provided the CDC awareness poster and a PrEP information pamphlet. Those are created by CDC so those are in the public domain. People are free to copy and to distribute those.

Then we move into enrollment and some places recommend a separate informed-consent process for PrEP. In my practice, I don't. We use it as part of the routine consent for medical treatment. So we don't have a separate consent, but some settings do just to make it something that they can monitor over time.

Adherence, as I mentioned, with the effectiveness. Adherence is critical. I mean, adherence is critical with many of the medications we prescribe. There is a publicly available system that's been created by the state of Oregon called oregonreminders.org. It's one example of a reminder system.

Patients or providers or social workers or support staff can go on oregonreminders.org. They can sign individual up or an individual can sign themselves up and they can get reminders, either through text, through telephone, or through email. And they can create their own reminders, put in their own content, and set it up with their own frequency.

And there have been some studies done with these types of SMS reminders. It shows that they significantly, substantially improve medication-taking behavior. And in the HIV treatment field, they're associated with reductions in viral load.

And then lastly I think, as part of a program, it's key to have monitoring, evaluation, and reporting. And on a monthly basis, the site should be aware of how many potentially eligible patients or clients may be seen. Of those eligible clients, how many have been offered PrEP? How many have been initiated to PrEP? And then what the outcomes are in terms of their STD tests or HIV tests.

And because we're still relatively new with the introduction and expansion of Truvada for PrEP in the United States, that kind of feedback and monitoring help sites understand what kind of impact they may be having, what kind of barriers may be identified, and then how to do quality improvement.

So routine HIV testing. So certainly, as part of offering PrEP, sites need to be comfortable with routinely offering HIV testing. The CDC recommends all persons age 13 to 64 years of age undergo at least one HIV test. They recommend that high-risk groups, like man who have sex with men and those with multiple partners or more than one partner, have at least annual testing. And in some individuals, more frequent testing. Up to two or even four times a year.

In my experience, having a clinic policy where it's explicitly stated that all patients should undergo HIV testing unless the patient declines-- what we call opt-out testing-- has been an important way for providers to feel comfortable routinely offering testing to every person they see. And that somewhat takes away some of the onus or responsibility from a provider, who can just say well, it's our clinic policy. Our clinic policy is every new patient, every patient who has no record of being tested, every patient who's in a high risk group needs to be tested.

It takes away some of the stigma. It takes away some of the challenges of the conversation. Someone may push back and say, well why are you testing me? Or, why are you offering testing? Because it's our clinic policy. Our clinic policy is that everyone that we see here gets tested.

It's also interesting to know that many patients think they've been tested for HIV when they actually haven't been tested. And they're surprised that they've given blood on an annual basis or when they're seen as a new patient and it did not include an HIV test. Because people often, in the community, think that providers always follow CDC recommendations or policies are always consistent with the best practices.

So let's go into our first case. So this is a 22-year-old man, recent syphilis treatment, who reports sex with other men. He tested HIV negative two months ago. And the questions are what additional history is needed? What tests are needed? And should Truvada for PrEP be prescribed?

So we're going to open it up and see if any of our participants would like to share their thoughts on this, either through the chat or through raising their hands.

MODERATOR: If you would like to chime in on this, please use the Raise Your Hand feature in the GoToWebinar toolbar, and we will unmute you. Or feel free to type comments in the chat section. So far we have no comments.

DR. JEFFREY KLAUSNER: Oh. Well, we'll get about 15 more seconds and if people don't have any comments we'll talk about some of these elements.

OK so in terms of additional history, so it's certainly relevant to know about the number of sex partners So he reports sex with other men, but how many other male partners has he had in the past 12 months? In the past three months?

Often, I want to know where he meets his sex partners. There needs to be an association with different types of sex partner meeting venues-- like online chat rooms, social media sites, the internet, sex clubs, bath houses, for example-- with increased risk for HIV. Plus, I'd want to know about his condom use and if he's a regular condom user or occasionally not able to use condoms. I'd want to know about other medication use and also his substance use. Certainly it's well known that substances, methamphetamine in particular, increase people's risk for HIV acquisition through both a biological and a behavioral mechanism.

And then, in terms of what tests, even though we tested HIV negative two months ago, we want to make sure that he's not HIV infected at the time that we want to prescribe the PrEP if we do. So we want to repeat an HIV test, and that should be with at least a fourth generation, which is the newest type of HIV test, or an HIV viral load assay.

We'd want to get a full battery of STD tests and, based on his exposure if he performs oral sex or has anal sex, ferential test for chlamydia and gonorrhea, rectal tests for chlamydia and gonorrhea, another syphilis test to look at his response to treatment. Also we'd want to get a hepatitis B test because, specifically, this current medication for PrEP Truvada also is active against hepatitis B. So it is important to know if you may be treating or inadvertently treating hepatitis B and then also know of someone at risk.

And then lastly should Truvada for PrEP be prescribed? Again that's going to depend on the risk behavior. But the CDC recommendations would say yes, that a young, sexually active man who has sex with other men with the recent syphilis infection meets the criteria for risk for HIV acquisition. And Truvada for PrEP should be prescribed.

So, polling question number three. You do get some more history. Yo do some tests. You do decide to prescribe PrEP and the patient wants to know when will protection from the Truvada likely occur. One day, three days, seven days, 14 days, or 28 days?

OK so most people think one to three days is too short. They'd be correct, and it seems to look like a least seven days. Some are 14 days and then drop off on 28 days.

So the data from the study suggests that at least seven days of use and after seven daily doses, people have an adequate blood level for protection. So that was done by different studies. They actually brought in healthy volunteers. They had them take medication on a daily basis and they measured blood levels.

And based on the data from a clinical trials, we know what blood levels seem to be adequately with protection. And people seem to meet the adequate level after seven days of use. So that's important in terms of counseling patients that they should not put themselves at risk for the first seven days. But after seven days, they would expect to be protected.

As I mentioned, the key onus on providers is to identify people at risk for HIV infection. And it's critical, in order to do that, that on a regular basis providers ask every man but they see if they have sex with men, women, or both in the past 12 months. And I found that particular phrase, "Do have sex with men, women, or both?" is the least filled with judgment, least inflammatory, very direct.

Often, yes, people are surprised but I always introduce it with a phrase like in order for me to help take care of you better, I need to ask some personal questions. Do you have sex with men, women, or both. And then I want to know about was this recent or not, so in the past 12 months.

And then, if they do have sex with men, we want to know a little bit more detail about their partnerships, relationships, and HIV status of partners. And in different studies that have been done in the United States, about 50% of men who have sex with men will have a steady or main partner.

And many of those men, certainly not all, will have some kind of agreement, or what we call a negotiated safety, with those regular main partners. They may agree to full monogamy, where neither partner has other partners. They may agree that they have an open relationship. They may agree that one partner has an open relationship. They may agree that they can have other partners together but not independently, so at the same time in terms of group sex.

And it shows some competency, on your part as a provider, in a nonjudgmental way to ask people whether they have an agreement with their main partner. Whether their partner has other partners, they have other partners, and what kind of status of that expectation and relationships are with their main partner.

Additionally, individuals may have a main partner. They also may have regular, occasional partners or, pardon the French, they may have fuck buddies. And these are people they may see on a regular basis, once a month, once a week, sometimes less often to have sex with. They may not be living with them. They may not be seen as a romantic main partner, but they may be regular partners that they may have sex with on an ongoing basis.

And then, thirdly, people may have casual or anonymous partners that they meet for one off sex, that they meet in clubs, online, et cetera. And there's really no regularity with that specific partner, but there might be regularity with meeting those types of partners. And the more one asks, the more comfortable one gets in talking about the types of partners.

And again, it starts to build trust and a sense of confidence between the patient and you, that you care about their sexual health and you're asking them some detailed questions about the type of partnerships. And this not only goes to build trust, but enables you to think about is this person at risk for HIV?

Certainly, if these sexual contacts are condomless-- and we've actually evolved some of the terminology. We don't talk about protected or unprotected anymore, we talk about condomless versus sex with a condom because people can be protected by the use of Truvada for PrEP now for HIV. So if people are having condomless encounter, it certainly increases their risk.

And then, we also I know about the HIV status of partners. So if people are having sex with partners who are positive or partners who are unknown status or not recently tested, that certainly would increase their risk for HIV acquisition.

And then, lastly, exchanging money or drugs for sex increases an individual's risk. And that also, potentially, opens the door to explore other social issues that may be relevant and important.

So the official CDC recommendations for PrEP use among men who have sex with men currently are an adult. They do not have acute or established HIV infection. They have had male partners in the past six months but they are not in a monogamous relationship. And, as I mentioned, it is important to understand what people mean by monogamous.

And then, in addition, that they have condomless anal sex or anal sex without a condom. They have had an STI. So in our case that patient had a recent syphilis infection. Or that they're in an ongoing sexual relationship with an HIV positive male partner.

And here's where we think about those research studies, which were done and discordant partnerships. And it also makes you think about non-MSM in terms of heterosexual men or women who may be in a partnership with someone who's HIV infected, the importance of making prevention available for them.

So this is the second case, a 42-year-old woman with an HIV-infected partner. Her partner's viral load is unknown. She has condomless sex when he's in town. So they're not living together all the time, but when he's around they have sex together.

So the questions are, is Truvada for PrEP indicated? What are some of the risks versus benefits? What kind of history and testing would be important for this woman? And we'll open up for about 30 seconds if people want to raise any questions or offer any comments.

MODERATOR: I did have one question that came in earlier that reads, do you think the amount of testing and monitoring recommended will make it too cumbersome for primary care providers?

DR. JEFFREY KLAUSNER: So the question's about the amount of testing and what's recommended. So right now, it is recommended that people are seen on a three-monthly basis and depending on how frequently other patients are seen with other chronic medical conditions, that may be an increase in the practice burden. And I don't think it would be too cumbersome, but it would increase the demand.

I think, when people get used to the ordering and the algorithms, they can create standing orders. So at UCLA, I have a standing order for, let's say, a new PrEP patient, which has a laundry list of tasks, and a follow-up PrEP patient, which has a subgroup of those tasks. So I can quickly, with the electronic medical record system, order that order set.

Also, the check in doesn't really have to take that long. And I actually think, once people get used to it on a regular basis, it will not be cumbersome.

OK. So case two. This woman has an HIV infected partner. The viral load is unknown. So I would say, yes Truvada for PrEP is indicated. The potential risks for this woman, there's some short-term side effects we talked about with nausea, potential weight loss. There's some small risk of longer-term adverse effects like decrease creatinine clearance and bone density, which are actually rare.

The benefits, clearly, if she takes a medication every day. She'll be protected against HIV from her partner.

Now one thing that makes it a little bit more interesting is that, if her partner is viraly suppressed-- so if her partner has an undetectable viral load-- there's very good data now that shows that her risk of acquiring HIV is essentially zero, so very, very, very low. So there may be less benefit to her if her HIV-infected partner is suppressed. But one would have to know that and one would have to feel confident that that individual remains suppressed.

And then in terms of baseline history, we already covered a lot of the tests that should be part of a standard baseline assessment. And we've also said that there hasn't been any reported risks in pregnancy. But for a woman, pregnancy testing would be indicated as well.

So in terms of identifying women at risk-- so again, as we're getting used to asking every male patient, every man if they have sex with men, women, or both. We want to ask if they're sexually active with men, about the types of partnerships, relationships, the status of the partner. If they have a steady main partner, what's the status of that main partner?

Does that main partner have other partners or other male partners? That's often something that people don't necessarily know, but sometimes they do know and they do know that their

main partner has other partners or other male partners. It would certainly, through the chain of transmission events, put them at increased risk.

Does a woman have other regular, occasional partners? To they have any casual or anonymous partners? Any exchanging of money or drugs for sex? And certainly injection drug use. And the CDC does specifically recommend Truvada for PrEP in active injection drug users.

And our third main population in terms of sexual behavior are men who have sex with women. And, similarly to heterosexual women, it has to do with the partnerships, the status of their female partners, whether they're female partners have other risks like injection drug use, whether potentially there's any exchange of money drugs for sex, or whether they themselves use injection drug use.

So it's key. Potentially I could share some instruments in the future, if people requested, of the simple check boxes and grids that many clinics use to identify the patient they see. If they have sex with men, women, or both; the number of partners in that period; and the HIV risk of those potential partners.

So the CDC recommendations for PrEP use by heterosexually active men and women, again adults. It's important to exclude current HIV infection. Sexually active and then not in a monogamous partnership.

Actually, those four bullets would capture a large number of people in the United States, but they have to have at least one of the additional following indications, that they are a man, they have both sex with men and women, that they're behaviorally bisexual, that they have sex with partners who are at substantial increased risk. So that partner is an injection drug user or that partner is bisexual.

And again this is going to be difficult to ascertain as many people will not know the risk behaviors of partners. And at this time no one's recommending to assume they have at-risk partners. The recommendation would be only to provide prescription if you know that they have at-risk partners. And then, thirdly, if they're in a discordant relationship with an HIV-positive partner, then it's recommended.

Then two more groups I just want to cover. Transgender adults-- increasingly, many primary care sites and clinics are asking individuals their gender identity. Remember that gender identity is different than their sex. So their sex is male or female, their gender is a man or woman. Now updated language is trans men or trans woman. People are asked their gender identity.

And then, among transgender adults, in terms of their sexual behavior with men and women or both and going through, again, the same algorithm about types of partners, relationships, and HIV status. And then any other specific risk behaviors they may have, such as exchange of money or drugs for sex, injection drug use. And then, because transgender persons tend to be

an increased risk for intimate partner violence, I often ask about any recent situations that might make one concerned for partner violence.

And then, lastly, is quite common for a transgendered persons to have, perhaps, not the most satisfactory interactions with health care and the medical system and providers. So I often open up a dialogue about that. How have they been treated?

And then, it's also important to ask what kind of pronoun would transgendered people like to be called? Would they prefer to be called he, she, by what name, et cetera. Because we can't and we can make any assumptions. And it is important to empower people, to enable them to give direction and make those choices.

All right let's move on to our next case, case three. So case three is a 36-year-old man with fever, chills, and a mild rash. He reports condomless, receptive anal sex three weeks ago at sex club. He's interested in PrEP. And there's an important point here that I want to bring up in terms of what might you, as a provider, be concerned about with someone who has symptoms of an acute illness but also recent exposure to HIV or other sexually transmitted diseases?

So what I'm particularly concerned about is acute HIV infection. And studies show about half of people who acquired HIV infection had some type of illness. And that may have been manifest with a fever, a rash-- not a very specific rash, a maculopapular rash. It could be on the chest or the back. There are some case reports of some of vesicular rashes but, generally, the rash looks like other viral exanthems, macular papillary lesions on the chest and back. A sore throat is not uncommon, headache, swollen glands, and diarrhea.

So people can feel anything from no symptoms to a mild illness to a severe illness, where they're actually bed ridden or go into an urgent care, emergency, or their provider for a medical evaluation. So it is important, particularly in people who may be at risk for acquiring HIV, to acquire about sexual risk behaviors that may have put them at risk.

And the concern, in terms of PrEP and the prescription of PrEP, is the HIV blood tests that are used may not always exclude the most recently acquired HIV, unless someone's doing an HIV viral load.

Let's move on the next polling question, number four. The question is about drug resistance.

So one thing that's come up among different policy makers and providers as the potential barrier to expansion of PrEP are people's concerns about drug resistance. And certainly, in today's day and age, that's a hot topic. Increases in bacterial drug resistance, and we hear about that a lot. So we don't want to be doing anything that may be associated with increasing drug resistance, particularly around HIV, that people may lose therapeutic options in the future.

So the question is, how common is HIV drug resistance among Truvada for PrEP users? There are at least hundreds reported cases. Resistance has never happened. It's rare and associated with poor adherence. Or, it's rare and associated with undiagnosed HIV.

OK so we do have a learning opportunity here, which is good. So the overwhelming majority picked "rare and usually associated with poor adherence," and a few people picked "rare and associated with undiagnosed HIV."

So actually the data show that it is indeed rare. However, it's usually associated with undiagnosed HIV. So if we look at these three trials, the iPrex trial, the Partners PrEP trial, and the TDF CDC trial and, if you look at the total on the bottom in column two, resistance among those infected in the enrollment, there were five people who developed a resistance at the time of enrollment.

And then there were 0 out of 75 who developed a resistant infection later on in the study. So when you add everything up in terms of the total, there were seven people with a resistance. Two were in a placebo arm, but five of those total seven had HIV. They actually had acute HIV before starting their Truvada. And that's why we must do the best we can to exclude acute HIV. So this was rare. PrEP was administered to, in all these studies, thousands of individuals. Resistance was rare, but when it did occur it occurred people who were infected at the time of initiation.

So the ways that we have to exclude infection at the time of an initiation is, one, a history. So is there any history suggestive of recent acute HIV infection? And that would usually mean a recent acute HIV infection in the past three or four weeks, which would be this clinical syndrome that I just described.

The second way is through the use of the most sensitive tests, like an HIV RNA assay. So it depends on what practice setting you're in. Some places may have an HIV RNA test available to exclude acute infection at the time of initiation. Other places may only have a fourth generation asset. So the systems are not necessarily the best, in terms of set up, to exclude acute infection. Although, as I mentioned, it is rare.

Just switching gears a little bit to talk about the clinical setting and the team, in routine primary care there seems to be better uptake among patients and better offerings by clinicians if there's a PrEP-friendly environment. What does that mean, a PrEP-friendly environment? It means to use posters like the CDC infographics that we made available.

This poster says, "What if there were a pill that could prevent HIV? There is. Ask your doctor." So something like that in the waiting area or in patient examination rooms. To have these pamphlets available, in terms of PrEP. Also, in our UCLA clinic, we have pictures, posters of different couples-- same-sex male couples, same-sex female couples, couples with different racial ethnic backgrounds-- just to show that this is an open and friendly environment and we accept all types of people of different sexual behaviors.

So just those images, actually, can go a long way to creating a PrEP-friendly environment. Also having staff made aware that we offer PrEP, that PrEP is highly effective, and it's an important tool to prevent HIV.

Secondly what's been useful is having someone on the staff-- it doesn't necessarily have to be a provider, but someone who's a PrEP champion-- who is kind of responsible for keeping up to date on the newest innovations in the use of PrEP for HIV, for making sure that the materials are routinely available. Often different types of staff-- whether it be nursing, answering medical staff, or registration staff-- sometimes know more about our patients than we do.

And they sometimes may make suggestions to providers about, hey, maybe you want talk to this person about PrEP. Because they often see who they come in with in the waiting room, who they leave with, and may interact with them at home in different ways than providers might.

Thirdly, increasingly people are adding different tools into the e-health system. So one thing is called a best practice advisory. So some of those best practices about routinely asking patients about their sexual behavior, their preferences in terms of gender of partners. And then, additionally, patients can do a self-risk assessment. So it's not uncommon for patients in the waiting room to have to go through these long surveys of recent symptoms or potential behavioral risk.

So make sure there's something included in there that captures social risk behavior that might make someone eligible for PrEP. And also actually look at those. I know sometimes people fill them out and then providers or staff don't necessarily look at those consistently, every time.

And then, fourthly, in a clinical setting, because Truvada for PrEP is costly, it is covered by, I can't say all, but by most medical care and pharmaceutical benefit plans. It's covered by many, Medicaid California, for example. It's covered by Medi-Cal. It's important that someone has a good, updated knowledge about what the coverage and the benefits are for PrEP.

So in terms of our typical clinical evaluation I've already mentioned some of these. I just summarized that one slide. To get this initial, at least a fourth generation HIV antibody antigen test with that antigen that contributes to the detection of early infection. Or, preferably, if it's available, an HIV RNA screening test which detects the actual virus and not just the body's reaction to it through the antibodies. This is the most sensitive test to detect recent infection.

STI screening tests for syphilis, rectal chlamydia and gonorrhea and ferential gonorrhea. Ferential chlamydia is not common. It's not recommended. Sometimes you can't do one test without the other. If you've got to do a ferential chlamydia test, that's OK. Hepatitis screening, if someone is susceptible to hepatitis B they should be vaccinated. Hepatitis C is also not rare in people who may have risk behavior for certain types of infections. And then baseline creatinine clearance or kidney-function testing.

And then to follow up, this is actually a little bit modified from what the CDC recommends, but everyone recommends HIV testing quarterly, pregnancy tests for women. So I recommend STI screening quarterly. The CDC only recommends it every six months, but we've found in our patient populations, where we're prescribing PrEP, very high rates of STIs and new STIs. So it's very important to screen and identify and treat those early.

Continued kidney function testing, that can be reduced to six monthly once it's demonstrated to be stable. And then people often ask about a bone scan because this very low incidence of bone mineral density loss but a bone scan is currently not recommended routinely as part of management.

So in terms of the prescription of Truvada, I recommend Truvada one tab daily by mouth, number 30. I give two refills, which will carry them to 90 days. Some providers give only that first 30 days and want to see them back in one month. I do see people back in one month anyway to review the dosing, adherence, and any side effects. We also want to manage any other interventions, vaccinations, et cetera, any referrals that might have been made to mental health or substance use.

And then it's important to think about, at least briefly, how you might do some risk reduction counseling. And because we have seen these high rates of other STIs, you want to ask people how to keep yourself at low risk from other STIs. And that may be through partner selection-- which is not particularly helpful-- frequent STI screening-- which is helpful-- and, certainly, condom use.

Because there is a very strong association between substance use and increased sexual risk behavior, I ask people, if they do endorse substance use, how does substance use impact their sexual risk behavior. And I found over the years that some people then can make a connection. And some people can engage in safer sex behavior when they anticipate they may be using particular substances such as methamphetamine, or something on the weekend.

And then it's important, as an outcome of this risk reduction counseling, that you and the patient at least identify one concrete step, one thing that they can do between now and next time they see you. Which might be something simple, like carry a condom with them when they go out, get an STD test, talk to a partner about their HIV or STD status, something simple and concrete to get them on a pathway to lower-risk behavior.

So it certainly comes up, in terms of medication assistance, what kind of programs are available for Truvada. So currently Gilead Sciences, the manufacturer of Truvada, will provide PrEP at no cost for individuals who qualify for assistance program, which is less than 500% poverty level income. There is a modest amount of documentation that needs to occur, and usually they'll last for six months and then they have to be recertified.

And the website's is on the bottom here, start.truvada.com. The criteria, they must be a US resident, must be uninsured or have no drug coverage in their current plan, HIV negative and

low income. There is a specific pharmacy that dispenses the medication. It's usually shipped to the prescriber. I have had some exceptions where it's been shipped to the actual patient, but usually it's the prescriber that must receive the medication. As I mentioned, it needs to be recertified on a six monthly basis.

Some of these issues are in somewhat flux, such as the shipping to the provider instead of the patient, and the frequency of recertification. So as this becomes more used and is there's a larger population, those indeed may change.

And then, secondly, Gilead also has a copay assistance program for insured patients. So right now the manufacturer is indeed trying to do what it can to reduce cost as a barrier. And that's why it's important for someone in the practice to have some familiarity with these programs and know how to access them.

So in terms of other programmatic support, the CDC has two published documents available on the website that talk about the clinical practice guidelines. Most of them we covered. And then it has a brief supplement for PrEP for the prevention of HIV in the United States.

The manufacturer Gilead has a bunch of different tools. Some of these tools have been used by providers, some have not. But it definitely has the registration materials for the medication assistance program. The agreement form has probably had less of an uptake.

So that's sort of an informal contract between the provider and the patient, that they'll take their medication, that they'll come back for their checkups, and that they'll reduce their sexual behavior with the condom use, for example. And then the provider checklist basically is a tool that covers a lot of the items that we went through in today's presentation.

Additional online resources-- I mentioned the things from the manufacturer which is Truvada and the CDC. Project Inform, which is an advocacy group in California also has some PrEP booklets and pamphlets. thebody.com, a popular website that we use in terms of learning about HIV and sharing information about HIV with patients, has some useful information.

And then PrEP Facts, which is a very user friendly, very simple language guide for the community or for patients, was put together by the San Francisco AIDS Foundation. It's called prepfacts.org. And all these items are freely available. And people can download these and use these as resources.

I did want to cover some of the issues that have been raised in the media. One is a statement by Michael Weinstein of the AIDS Healthcare Foundation that PrEP is a party drug, and that PrEP users are party whores, and that people engaged in PrEP and use PrEP somehow have some moral issues. And it's very interesting. This kind of rhetoric is very similar to what we hear around oral contraceptives or any kind of contraceptives, as a matter of fact, by certain groups.

And I think you have to check your own assumptions as a provider and think about what's best for the patient right there in front of you. And people do take risks and now we have a medication available that will reduce their risk. Certainly, if people did not have sex or people were wholly monogamous or people used condoms 100% percent of the time, people would not be getting STDs and HIV.

So in my practice, I often think about [? harm ?] reduction and trying to make interventions available for people that will reduce their risk. And certainly PrEP is a way that people can reduce their risk.

And then, on the flip side, you see advocacy from the community. Talks about people can be responsible, people can take the medication. It works very well if they take it. So there's been a push back from the community against some these attitudes and stigmatization of PrEP as a party drug.

So I just included this slide with my contact information. And also, if people have large practices or expect they're going to see, or even want some help, any help. I've had some very good support from people in medical sciences, of Gilead Sciences, the manufacturer.

And these are just two people I've worked with over the past year, Brian Palmer and Olga Lugo-Torres. They divide up the country regionally, so depending on where you are they may be the appropriate medical science representative for you.

They're both doctors. They have good access. They're happy to come in to different settings and do additional training, provide additional tools. And I found a very good resource that were very helpful to me in setting up PrEP at the AIDS Project Los Angeles program and then in my own practice here in Los Angeles.

So thank you very much. I'm going to stop there. And we certainly have a few minutes for questions.

MODERATOR: If you have any questions or comments for Dr. Klausner, now would be the time. You could raise your hand and we'll unmute and you can ask a question verbally or you can type your question into the questions pane on the GoToWebinar toolbar.

We have one comment. It says thank you.

DR. JEFFREY KLAUSNER: You're welcome.

I also have a colleague with me here, Jeremy Chow who is an infectious disease in HIV fellow at UCLA. So Jeremy's available to answer questions as well.

MODERATOR: We have one question that reads, who do you think primary care providers will trust that they can and should do this? I'm not exactly sure what they mean by that.

DR. JEFFREY KLAUSNER: So in terms of trust at the patient level or in terms of policy makers and the CDC, why are we focused on primary care?

So I think, from the patient level, part of having a therapeutic relationship is to have trust with someone. Talk to them about the risks, benefits, and alternatives to these kinds of treatments and seeing if it works for them.

I mean, ultimately, it comes down to a one on one interaction between the provider and the patient in terms of what works for them. And building trust through being nonjudgmental, asking relevant questions, and caring about patients I think would go a long way.

In terms of the policymakers and the CDC, et cetera, we think that just providing PrEP in STD clinics or HIV clinics is going to miss an important proportion of the population at risk. And from our case reporting data, there's about 45,000 new HIV cases a year in the United States. Many of those never accessed STD services or HIV prevention services or LGBT call services. But, yes, they've been accessing primary care.

So primary care, particularly in federally-funded sites and sites in the southeast, where we have the least control the HIV epidemic in the southeast part of the United States. They're really seen as kind of the front line of HIV prevention. In other urban areas-- New York, San, Francisco Chicago, LA-- that may be less so, but many parts of the country do not have culturally-competent, community-based LGBT services. So the only place people are interfacing are with primary care.

MODERATOR: OK we have another question. Is there any way to identify HIV-friendly physicians?

DR. JEFFREY KLAUSNER: Yes.

I would say yes. I mean, there are. The Gay and Lesbian Medical Association has a list of providers. There's also American Academy of HIV Medicine has a list of HIV providers by states. Often major universities in the area, those universities will have an HIV clinic or HIV treatment programs. Such a good resource to contact.

Not directly related to PrEP, but these Gilead medical representatives would also know who are high prescribers of HIV medication and who has a good reputation. I mean we often work through a network of each other. We do a lot of cross referral. So that would be one way to actively find somebody.

The second thing, if I were a patient I would look for cultural competence in my physician. Are they asking me about my sexual behavior? Are they nonjudgmental in terms of my partnership choices? What's their kind of reaction when I tell him? And do I feel that the information is confidential? And is it being received in a nonjudgmental manner?

MODERATOR: OK thanks.

If there any other questions, please enter them in the questions pane. If not, then I want to thank everyone for participating in today's webinar. We hope that you're able to find the information provided useful as you continue your P4C project and take a few moments to complete the feedback survey that you will receive at the close of this webinar. It will also be made available to you in a follow-up email.

Thank you again for participating in today's webinar. And thank you Doctor Klausner for the excellent presentation.

If you have any additional questions or comments that need to be addressed, please email us at p4chivtac@mayatech.com.

OK take care everybody, and we'll see you next time.

DR. JEFFREY KLAUSNER: Bye. Thank you.