WEBINAR VIDEO TRANSCRIPT

Partnership for Care HIV TAC

The Integration of PrEP in Clinical Practice

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CHELSEA WHITE: Hi everyone, this is Chelsea White, welcome to our webinar, The Integration of PrEP in Clinical Practice. Today we will have two presenters. Our presenters are Dr. Dawn K. Smith and Dr. Karen Hoover.

My name is Chelsea White and I am one of the two training and technical assistance specialists for the P4C project. Dr Smith is a medical epidemiologist in a division of HIV/AIDS prevention at the US Centers for Disease Control and Prevention, where she served as biomedical interventions activity lead in the epidemiology branch, and conducts activities supporting the implementation of daily oral antiretroviral pre-exposure prophylaxis, PrEP, and other biomedical interventions to reduce rates of new HIV infections in the US. In that role she led the development of PHS clinical practice guidelines for PrEP.

Dr. Karen Hoover leads the health services research for prevention with negative pain in the division of HIV/AIDS prevention at CDC. Prior to joining CHAP, Karen was a health services researcher in the division of STD prevention at CDC. Karen's research interests include HIV testing and linkage to care, biomedical HIV prevention, including pre and post exposure prophylaxis and male circumcision, access, utilization, quality, and cost of HIV and reproductive health services, elimination of MTCT of HIV and syphilis, the US HIV and STD health care safety net, HIV and syphilis diagnostics, and development of novel models for sexual and reproductive health services.

DAWN SMITH: Good afternoon everyone. As a family practitioner, I'm particularly excited to be able to talk about PrEP and how it can be integrated into primary care practice. One of the reasons why the Centers for Disease Control is so invested in scaling our pre-exposure prophylaxis is because of the number of new HIV infections that are still occurring in the United States. For more than a decade we've had about 50,000 new: infections each year, and while that represents success in terms of bringing down the extremely high rates from the early ages of the epidemic, we clearly need additional tools in order to make further progress.

Among those who are estimated to have new infections in 2010 the most recent year for which we have data, you will see that men who have sex with men constitute the largest group of persons who are becoming infected with HIV, followed by black heterosexual men and women. And then smaller numbers of other heterosexual populations and injection drug users. Among MSM, we're having a specific problem with young MSM. So MSM between the ages of 13 and 24 actually have increasing rates of HIV infection, as compared to other groups which have

either stable or falling rates of HIV infection. And among young MSM, this is particularly marked for black young MSM.

So for these, because this problem is occur ... [AUDIO DROP OUT] … populations. So for MSM there was a trial done in six countries, on four continents, in which participants were given a daily dose of Tenofovir and emtricitabine. This is marketed in the US as Truvada. And in the I PrEP study preparing those who were randomized to the drug and those were randomized to placebo, those randomized to drug had 44% fewer HIV infections. But when the analysis was redone by measuring the presence of drug in blood indicating adherence to the dosing, among those who had drug detected in their blood, there were 92% fewer infections than those in the placebo arm.

Similar analyses were done in a large trial for heterosexual discordant couples, in which the positive partner was not yet eligible for treatment, in which overall there was a 75% reduction associated with taking Truvada daily. And among those who had drug detected, the reduction in risk was 90%.

A study was done in Thailand with people who inject drugs using Tenofovir alone, and on average they saw 49% reduction, and among those who had … [AUDIO DROP OUT] … drug detected it was a 70% reduction. Those results indicated to us that PrEP can be highly effective but it's very dependent on adherence. And in trials, adherence is likely to be a little bit different than it is in community practice.

So a set of additional studies were done after the trials that showed effectiveness. In a study with MSM, in which they provided people who had previously been in the trial, whether they were in the placebo arm or the active arm they were both offered daily oral prophylaxis. On follow up what they saw was that those who had drug levels associated with not taking drug at all, had an HIV incidence of 4.7 per 100 person years. Among those who had drug levels associated with taking four or more pills per week, there were no infections observed and there was a clear dose response relationship in terms of adherence.

In a study done in the United States, with MSM recruited in STD clinics in three cities, it was clear that achieving high adherence can be done in this population in the US, again using blood levels and looking only at those who had the highest efficacy associated with four or more doses per week. On average 3/4 of the men were able to consistently take their drug, although there was variation in the sites. So based on these and other data in 2014 the Public Health Service issued guidelines for the clinical use of daily oral PrEP in the United States. And we recommended PrEP to be implemented as one prevention option for people at substantial risk for HIV infection, including MSM heterosexually active men and women, and injection drug users.

These two drugs are cleared in the kidney. This is important and that they're not metabolized in the liver. This is important because it affects both, some of the concerns about side effects and toxicity, and also some of the issues around drug interactions. There are no drug interactions of these drugs with hormonal contraception, with STI medications, or with medication assisted

therapies for injection drug use. Both of these drugs have been widely used in treatment regiments with HIV positive women, who subsequently completed pregnancies. And in the pregnancy registry, as well as in women in the trials who became pregnant, there are no safety signals identified. And these drugs appear to be safe in both pregnancy and breastfeeding.

There are two additional concerns associated with Tenofovir in particular. One is, that in the people who have HIV infection, and are taking Tenofovir containing treatment regimens, there have been observed renal incidents that gave pause, in terms of giving this drug to uninfected people. However in the IDU trial for example, in none of the trials has there been any serious renal outcomes, and this is one example. In the IDU trial where people were on the drug for as long as five years, you can see that there was a very modest decline in the estimated GSR, but it didn't even come close to the level at which we would consider it important to stop Tenofovir which is 60 mls per minute. So even over a fairly long period of time in uninfected people this appeared to be a safe drug.

Similarly in positive, there's been a concern about the effect of Tenofovir on bone mineral density. In these slides on the right what you see in the blue are declines in bone mineral density among positive patients in several trials, in green you see bone mineral density in persons in PrEP trials. And what you see for persons in PrEP trials, is a very modest decline in bone mineral density that stabilizes fairly quickly. In follow up studies it returns to the baseline when Tenofovir is completed, and there is no associated increase in atraumatic fractures.

The last issue that has been considered a safety issue in PrEP is whether persons who are taking PrEP would increase their risk behavior in ways that might increase their HIV infection rates despite taking PrEP. In the trials, there has not been seen any kind of risk compensation for both sexual behavior and injection risk, levels of risk behavior went down and stayed down during the trials. This will need to be followed as we implement this in the community since trials may not perfectly predict what will happen in community use.

So as we think about implementing PrEP, one of the first questions is, who is it who should be providing this, given that we're talking about people without HIV infection. So while HIV care providers have the most experience with these drugs and are experienced in providing health care for HIV infection to the same populations, it is uncommon for uninfected people to seek their primary medical care from an HIV care provider. And so in addition to prep being provided by some HIV care providers, we are working very hard to be sure that there are STD care providers, drug treatment care providers, and primary care providers, who are knowledgeable and prepared to provide PrEP to their uninfected patients when indicated.

The first step in configuring PrEP obviously is to decide which of the patients in a practice are appropriate for PrEP, have indications for PrEP. And that involves taking a brief sexual history to ask patients whether they are sexually active with men, women or both, what consistency they use condoms, whether they know they have an HIV positive partner, the number of sexual partners that they have, and any history of recent STIs. For drug use, we would like to know whether they have a history of injection drug use and what their drug treatment history is, because drug treatment is often interrupted by periods of relapse.

And last, we'd like to know something about their most recent potential HIV exposure, because some patients with a very recent exposure may need to start on non-occupational post exposure prophylaxis, rather than pre exposure prophylaxis. In addition, there are some conditions that would give you either a contraindication or some pause in prescribing Tenofovir and entricitabine. The primary one is to know the HIV testing history of the person. We'll talk a little bit more about this, but clearly this is for people who do not have HIV infection.

These two drugs are not sufficient for people with infections. So you need to understand when is the most recent HIV test this person has had. In addition, you want to look at recent signs and symptoms of an acute viral illness that might represent acute HIV infection. Patients who have preexisting significant renal or bone disease are probably not good candidates for these medications, and similarly patients who are on drugs that are known to be nephrotoxic may not respond well to a Tenofovir containing regimen.

So the initial laboratory testing before placing that person on PrEP involves confirming that they're HIV negative, confirming that they have normal renal function and checking for hepatitis B serology, if they're not known to be vaccinated. The reason for doing this is not to determine whether they're eligible for these PrEP medications, but because Tenofovir and emtricitabine are active against hepatitis B, you would want to know if a patient had chronic hepatitis B infection, so that when they're ready to transition from PrEP to some other form of HIV prevention, you can monitor them for flares of their hepatitis and intervene quickly if you see them.

You want to do pregnancy tests for women to be sure not to exclude them from PrEP, but so that you can counsel them appropriately about PrEP use in pregnancy. And you want to do STI testing, including extragenital testing for MSM. My colleague Doctor Hoover, will talk more about providing PrEP to women, including the context of pregnancy. In the HIV testing, we work very much to exclude people who have acute HIV infection, and for that reason we strongly prefer to use a fourth generation antigen antibody test because they are very sensitive to early infection.

While some practitioners like to do viral load tests, if you get a very low positive viral load, sometimes these have been false positives, and so in general we prefer the fourth generation antigen antibody tests, but viral load tests are acceptable. By the way, oral tests are not sufficiently sensitive and should never be used to determine that someone is negative for the purposes of starting PrEP. So in the guidelines we have this algorithm recognizing that both their clinical preferences and their differences in the availability of some assay.

And so people should first have an antibody assay blood specimen. If that test is negative, then signs and symptoms of acute infection should be sought. If they do not have any evidence of a very recent viral syndrome, then you can go ahead and start PrEP. If they do have any indication that concerns you about acute HIV infection, then either do a fourth generation antigen antibody test, do a viral load test or because this is not an emergency procedure, you do have the option to bring them back in another month, retest with an antibody test if that's the only

test that you have available. That's not really a preferred option because during that month they may have additional exposures and you can end up chasing your tail.

So when you're ready to begin PrEP, what you would do is prescribe Truvada to be taken once daily. Both the FDA and the PHF guidelines suggest no more than a 90 day supply. This is so that you can ensure the availability of the patient for repeat HIV testing. It's important to educate patients about what side effects they might have and what the management of those side effects would be, because it supports adherence through an early start up syndrome that sometimes occurs.

As with all medications you'd like to provide them with some adherence to education and counseling. You also want to talk to them about their safer sex and injection behaviors and as with most health care, you want to be sure that you provide them with the assistance for insurance and medication assistance programs that may be useful to cover the cost of their medications and clinic visits. And then schedule a follow up visit in three months. Some providers prefer to see patients who are beginning PrEP sooner, so that they can reinforce the daily pill taking, and help to manage the side effects et cetera.

For follow up visits, you want to repeat the HIV test every three months. This is really important, because one of the concerns about antiretroviral used in this manner is a concern about generating resistance. In the trial, the only resistance that was seen was in patients who had acute HIV infection were thought to be negative and were started on PrEP. [INAUDIBLE] at three months and then every six months, a pregnancy test every three months and STI tests every six months even if asymptomatic. STI tests may be indicated more often for some patients, but at minimum every six months.

At these visits, you should assess their experience with adherence and help them to improve their adherence if they're having problems. And you want to talk with them about their risk and protective behaviors. If they remain negative and it appears to be safe and still indicated, then prescribe another 90 days of Truvada and schedule another follow up visit in three months. This is explaining the resistance issue and that is, if people are not taking the drug, then they are likely to get infected but they are not likely to get resistance because there's no direct pressure.

In the green on the right if they're taking all of their drug, they're very unlikely to get infected and unless they are infected, there's no virus to be resistant. There is a zone in the middle where they're taking too little drug to block infection completely, but enough drug to apply drug pressure in which resistance may develop. This window seems to be fairly small in all the follow up studies, there has been very little resistance. Only to emtricitabine, none to Truvada, to Tenofovir in patients who became infected after they started taking PrEP.

In terms of supporting medication adherence there are things that we know from chronic care conditions, from HIV treatment as well as from PrEP. So in the importance of explaining to people what side effects they might expect and how to manage them. In the case of PrEP somewhere to 8 to 10% of patients in the trials experienced a start up syndrome that involved nausea, mild abdominal pain and maybe a little diarrhea. It resolved over two to three weeks.

These things can be managed with over the counter medications and it's reassuring to patients to know that this is not going to go on for a long time.

Assess past issues with pill adherence and then suggest adherence methods that are related to whatever problems they seem to be having. The most common reason for non adherence is forgetting to take your pills and so things like pill boxes or putting your pills next your bedside light or putting your pills next to your toothbrush, are things that help people. Side effects is the second most common. This can sometimes be resolved by taking it before you go to sleep. And the third most common reason is people being away from home and forgetting to take their pills with them.

When it's time to discontinue PrEP this can occur for two reasons. Number one is a person becomes HIV infected and in that case people should be offered immediate transition to a treatment regimen, and you should document they're HIV resistance test results. For people who remain negative and who have decided that PrEP is not what they want to use for prevention, then you need to document their HIV and creatinine test results when they're coming off PrEP. Assure that they have a prevention plan in place for other activities to reduce their risk. And if they have chronic hepatitis B infection, make sure that you monitor their liver function and provide adequate treatment if a flare occurs.

One major concern of a lot of the community about PrEP, have to do with the cost of the medication. PrEP is covered by most public and private insurers, most Medicaid programs and for those who have high copays there is a copay assistance card available from Gilead Sciences and there are copay assistance grants available from the PAN foundation.

For those who have low income and no insurance and by low income is defined in this case as less than 500% of the federal poverty level, and no insurance coverage, Gilead Sciences will provide though their medication assistance program, free Truvada to the clinical provider, to give to the patient. So between the coverage of insurers and the medication assistance program, there are very few patients who cannot afford PrEP.

In addition, some jurisdictions have provided their own assistance programs. So in New York for example, they have an assistance program that's. not for the drug, it's for uninsured persons to cover the cost of clinical visits. This is an example of the patient assistance program. The thing to notice is that in order to use this, you need to be a resident in the United States but you do not need to be a citizen or Visa holder. So these forms get completed by the provider of a clinic, faxed to Gilead Sciences and then they arrange for the medication to be delivered. There are certain populations that have special issues related to PrEP and they include adolescent minors. There is no reason to believe that these drugs are unsafe for adolescents. They are widely used for treatment, for example for pediatric patients as well as adolescents.

However, the ability to consent for medical care without parental consent, is an issue for adolescent minors to receive PrEP. And so you need to be aware of what the age and regulations are in your jurisdiction. There's the issue of pregnancy and you'll hear more about that in a little while. For corrections population, these are sometimes brought up as an issue.

This is probably only important in terms of [INAUDIBLE] unlikely that PrEP would be provided in prison itself. And there are special issues for persons who inject drugs.

So, there was a study done specifically looking at what is the role of prepping HIV discordant couples when treatment is available for the positive partner. That study is ongoing and what they saw that was really interesting was first of all PrEP uptake was higher than treatment uptake. In this study they continue negative patients on PrEP until their partner is completely virally suppressed. And then a follow up time that had been accrued at the time of this report, nearly half of the patient time was spent on PrEP alone, about a quarter was spent with both PrEP and ART overlapping and only 16% of ART alone. What they show was a 96% reduction in HIV incidence. So PrEP can be very useful in HIV discordant couples, both in the early phases of treatment for positive partners but also where positive partners are not on treatment.

For conception and pregnancy, there are a couple of things to keep in mind. It's important to maximize viral suppression in the positive partner to diagnose and treat STIs in both partners, and then to consider whether fertility assessments are indicated. You need to consider all feasible safer conception options and if PrEP is decided to be the best option, begin PrEP one month before attempts to conceive, time attempts to conceive to peri-ovulation days, and if there is no conception, continue PrEP for one month after the last condomless sex. If the woman, if it's a negative woman and she conceives, or she's already pregnant at the time that you see them to consider about PrEP, it's important to consider continuing PrEP through the pregnancy because we know that pregnancy renders women more susceptible to HIV infection. And if a woman becomes infected, she's much more likely to transmit to her baby.

For people who inject drugs, it's indicated for uninfected patients who themselves are drug injectors, or are sexual partners of a drug injector, as well as those who have a positive partner who may or may not inject drugs. Important in terms of adherence for PrEP medication. So whether that's buprenorphine or methadone, these methods are highly effective in reducing injection and will improve adherence to [INAUDIBLE] that as well as directly affect their risk of [INAUDIBLE], although it does have some forgiveness for missed doses. You can successfully reduce any HIV infection risk substantially, both by injection or by sexual activity. In addition, there's some observational evidence that may reduce hepatitis [INAUDIBLE] young men that don't regularly [INAUDIBLE] access preventive health care. However it does not [INAUDIBLE] missions that are associated with some risk behaviors, like commercial sex worker or homelessness.

There are a few key challenges for PrEP in primary care settings. The first is that many primary care practitioners are not aware of PrEP or don't know about how to prescribe it. Some are uncertain about whether this is something the primary care docs should do, or whether all PrEP persons should be referred to an infectious disease clinic. In some cases there's a problem of lack of support from clinic and leadership, so there may be one or two practitioners who are very interested in PrEP but without leadership support they find it difficult to implement. And often we're told that there's not a protocol that's tailored to the clinical flow, that's compatible with a primary care practice.

In terms of primary care one of the points that I want to make you is, sometimes I hear, this is too complicated. I can't, I can't do this. This is not a primary care practice. As a family practitioner, it occurred to me that this is really no more complicated than what we already do, for example to treat prediabetes. So I'm not going to go through this slide in great detail, but again if you look at what every primary care practitioner will do in the process of prescribing metformin, and then you look at what we're asking to be done to prescribe PrEP, it's really pretty compatible. There's diagnostic tests there's counseling that you want to do with the patients about risk behaviors, there's periodic clinical assessments, adherence is a problem for both the drugs. This is something that primary care practitioners can do, but we have to help them to be more comfortable doing it.

One of the ways that we're trying, is that we've established a PrEP consultation line, in which providers can get clinical advice Monday through Friday from 11:00 to 6:00 eastern time and voice mail at other times during the day. The staff at this clinical center, includes the ID docs, family physicians, pharmacists, obstetricians, internists, a whole variety of practitioners who are very expert in antiretroviral use for both treatment and prevention, and they can provide advice on all the steps involved in providing PrEP to patients. We hope that doing this will help us to bring down the number of new HIV infection in the United States.

This is an example of a modeling study that looked just to providing PrEP for MSM in New York City, but we hope to see similar impact on all the populations for whom PrEP can be useful. Again this is for your reference, but these are some places that you can go for resources about how to provide PrEP, how to get medication assistance coverage and how to get more information either for yourself or for your patient. So Dr Hoover will now talk to you about PrEP in women. And then we had a couple of case studies that we wanted to try to get to. We'll see if we have time.

KAREN HOOVER: Wonderful, so thank you Dr. Smith, that was a really great presentation and I hope that the primary care providers in the audience agree with us that PrEP is something that you should be implementing in your practice for high risk patients. So I'm just going to talk a little bit more about women and PrEP and so this slide shows the numbers. I think you've seen this slide. Dawn showed this at the beginning of her presentation. It just looks a [INAUDIBLE].

Women also bear a significant burden. And I think we all know that HIV diagnoses in women have been decreasing over the past several years. But they still work out to a significant proportion of all infections. And while this slide doesn't show you the data, in 2013, in the United States 20%, which was over 9,000 of the estimated 47,000 plus diagnosed HIV infections were in women. Most of these infections were from heterosexual contact, rather than injection drug use.

So this figure is from our HIV surveillance report and it shows that while black women comprise only 13% of the US population of women, they're disproportionately burdened with 63% of new HIV diagnoses. So given that most new HIV infections are overwhelmingly in men who have sex with men, why are so many new infections diagnosed in women? Why are women at

risk? And there are several factors that probably contribute to the large number of infections in women, and I've listed some of them here and I'll discuss them in a little bit more detail.

First, their social and sexual network might have a high prevalence of HIV. They can also be unaware of their male partners status and women often engage in high risk sexual behaviors that put them at risk for HIV acquisition. They might lack the control or are unable to negotiate with their partners to use condoms. And finally asymptomatic sexually transmitted infections are common in both men and women, in that if they're left undiagnosed and untreated they can facilitate HIV transmission.

So this network is from a study by Hurt and colleagues in North Carolina and it was constructed based on an HIV outbreak investigation among black MSM. And if you look closely at the open triangles that represent HIV negative women, you can see that these women have several sexual partnerships with MSM's that have both acute, depicted in red dots and established, with the yellow dots, HIV infection. And as a part of this sexual network, it's apparent that these women are at risk of acquiring infection.

So we know that women often choose partners within their community, and if women are in a population or geographic location with a high prevalence of infection, the risk of exposure to HIV during sex is increased, And as previously mentioned, women might not be aware of their partner's HIV status, as was likely the case with many of the women in this network.

So the risk of acquiring an HIV infection, varies with the type of exposure as shown in this table. As the receptive sexual partner, women are a high risk for HIV acquisition with vaginal sex, and an even higher risk with anal sex. And among young US women, sex has become common with almost 40% reporting it in the most recently analyzed cycle of the National Survey of Family Growth, NSFG, shown on this slide. NSFG is a survey that CDC conducts, and it provides a nationally representative data on reproductive and sexual behavior of US men and women of reproductive age.

So we also know that condoms are highly effective in preventing transmission of HIV but only when used consistently and correctly. In relationships women often lack the control that's necessary to prevent an exposure. They are sometimes unable to negotiate safer sex practices such a condom use, that requires the participation of her partner. So PrEP is a really great new tool that gives women the control to prevent acquisition of infection. And it doesn't depend on her partner.

And then finally, sexually transmitted infections can increase the risk of both transmission and acquisition of HIV. And although really common, they're often undiagnosed in both men and women because they're asymptomatic. Many studies have found that routine screening of asymptomatic persons, as is recommended by national guidelines, is typically very low. And STIs do matter with HIV transmission in women. These data are from a recent study that found women in Florida with STIs had higher rates of HIV seroconversion than women without an STI. It was as high as 598 per 100,000 person years among women with syphilis, and 171 among women with gonorrhea compared to only 30 a month without STIs. But if you notice that, the

study found that most HIV diagnoses almost 90% of them were among women without an STI underscoring the challenge in identifying at risk women who would benefit from prevention.

I'm just going to turn for a moment to PrEP section. I think Dawn's done a really great job of covering a lot of the key points. I'm just going to quickly repeat a few of them, because I think they're important.

So obviously discordant couples who want to become pregnant, have several options to prevent transmission while we can see, even I think Dawns' alluded to these. Either of the infected partners can receive treatment as prevention, resulting in suppression of the viral load. Couples can limit their attempts to conceive around the time of ovulation, so that carefully timed conception attempts exposure can be limited. STI testing and treatment can decrease the risk of transmission.

And then for the positive woman with a negative partner intrauterine or intervaginal insemination or male circumcision are options. For the negative woman with a positive partner, sperm washing with insemination or intercytoplasmic sperm injection, is an option but only after the sperm have been tested for the presence of HIV RNA.

So PrEP is also an option of course to prevent transmission during conception both for the unaffected male or female. And Dawn I think already mentioned that uninfected women are more susceptible to becoming infected during pregnancy. So it might be a good idea to continue PrEP throughout the pregnancy. And I think Dawn also mentioned that if a woman becomes acutely infected during pregnancy, her risk of transmission to a fetus is greatly increased because of the very high viral loads that we have in acute infection.

And also back to what Dawn had said, I want to just once again reassure you that we have ample data that supports the safety and efficacy of Truvada during pregnancy. So apart from PrEP-ception, I think it's really challenging to know which women are at a substantial risk for acquiring infection and who we should offer PrEP to. And this is a really important area for research, to help us to understand who these women are so that it can inform the development of tools and interventions to identify them.

Well here a few suggestions for women who might benefit from PrEP and these are not entirely evidence based but just thoughts that might be helpful while we wait for more definitive data. So I think we might want to offer PrEP to women who are concerned about becoming HIV infected. For women who have an HIV infected partner and I think we have really [INAUDIBLE] to support that, and I think women who are in a community or network with a high prevalence of HIV are also potential candidates for PrEP. And I think it's the high network prevalence that's probably a key factor that's causing the disproportionate rates that we observe among black women that I described a few slides ago. Women without STIs, especially syphilis or gonorrhea, might be offered PrEP. And as I've mentioned STIs are both a biomarker for risk and also a co-factor for transmission.

And then finally if women report a history of a high risk sexual behavior such as anal sex or if they've been diagnosed with rectal chlamydia or gonococcal infection, PrEP might be discussed with these women as well.

So just going to really quickly mention the vaginal microbicides trials and just point out that we are kind of back to the drawing board with non-oral PrEP options and I'm not going to spend a lot of time on them because I want to give us plenty of time for our case studies. And just to point out that there are things on the horizon for women and for future potential delivery methods including vaginal rings that are in clinical trial. They've released the [INAUDIBLE] ring and it might be an option and potentially long acting PrEP injection medication. And although really not currently in development, but perhaps being conceptualized, are implantable PrEP agents, kind of analogous to contraceptive device, the contraceptive implant [INAUDIBLE] device [INAUDIBLE] that might be able to use formulations of Tenofovir pro-drugs that would permit sustained long term use. And all of these methods can become can be combined with hormonal contraception, which would be a really great option for women.

And so I'm just going to, just a couple more slides. I think we can accelerate PrEP implementation for women by focusing efforts on their health care providers and OB/GYN offices, family planning clinics, FQHCs, primary care offices, STD clinics, all venues for women to seek health care. And we can support education of these providers with academic and repeated academic detailing. And also disseminate tools for these providers to assist in PrEP care. But Dawn's already pointed out that we also need to educate women about PrEP, so that we can create some patient demand for PrEP and help them to understand how it can be very protective for them at various times in their lives.

And then finally echoing some of Dawn's points, increasing implementation starts with understanding the barriers. And this slide lists some of the barriers at both the patient and provider level. Women are unaware of PrEP. They can be concerned about PrEP medication side effects. I think Dawn has told you that these are usually temporary and manageable. They're also concerned about stigma associated with taking HIV medications and concerned that if they're taking medication like Truvada, a potential partner, friend, or family member might perceive that they're infected.

And as [INAUDIBLE] has also talked a lot about the concern about access and affordability. And also the health care providers are surprisingly unaware of PrEP. It's a new agent I think that awareness is increasing. Then Dawn's also talked about inexperience and concern with prescribing HIV medication. Also concerns about risk compensation and increasing rates of STIs in PrEP users. And then finally it's really necessary to conduct a sexual risk assessment, asking a lot of questions about sexual behavior. And this is really hard for providers to do when they have limited time during a visit and it can be uncomfortable for both patient and provider and it often is not performed at visits.

So, I think I'm all set and I hope we're going to have time for the case study.

DAWN SMITH: So I guess the first thing before we do the case studies, are there PrEP questions from the audience? We've been talking at you for quite a while now.

CHELSEA WHITE: This is Chelsea. Karen what I'll do now is I will check for questions and then we'll let you know. And you can type in your question and then I will read that out loud. You can either click the hand raising icon or select the questions or you can select question and then type in your question and I can read both questions aloud. OK someone has entered that they would give him an HIV test first.

DAWN SMITH: Absolutely. Absolutely important. And so if his HIV test is negative, and let's say while you're drawing the blood you go ahead and do your creatinine testing, so his creatinine test is normal. Is there anything about this patient that makes you think you might not want to give him PrEP?

CHELSEA WHITE: OK, I'll wait for a response. Again you can type in your response in the question box. A person wrote, we would give him PrEP. Then the next question asks what if they are seroconverting?

DAWN SMITH: Well, what test would you do to find out if they're seroconverting?

CHELSEA WHITE: Another person suggested maybe do full STI panel.

DAWN SMITH: Sounds good

CHELSEA WHITE: OK I'll continue to wait for other people to respond.

KAREN HOOVER: It's really important to test for the STIs, even though you might want to give this person PrEP because as we've discussed the STIs can facilitate transmission and acquisition of HIV and so it's really important to diagnose and treat them to get a little bit of synergy with our prevention efforts.

DAWN SMITH: But also for the benefit of their health.

KAREN HOOVER: That's right. That's right.

DAWN SMITH: We don't want people walking around with undiagnosed STIs.

KAREN HOOVER: That's right.

DAWN SMITH: OK so everybody seems right on target about the primary care issues for this young sexually active man. The other thing I would say is that it might be important to try to encourage him to use condoms more often, both for his STD because PrEP will not protect him from STIs and if he can always use them with female partners then he's at least shown the capability to use condoms. So that would be the other thing to address with him.

KAREN HOOVER: And I think that he consistently uses condoms with females is maybe a good sign that he's going to be adherent with his PrEP. [INAUDIBLE] if he's careful.

CHELSEA WHITE: OK Someone mentioned whether or not you can speak to the importance of medication adherence.

DAWN SMITH: Well I think as the clinical trial results showed just like any other medication, if you don't take it, it won't protect you, it won't do its job. So medication adherence is very important in this case, as it is for many other medication regimens. If people are going to rely on PrEP as a big part of their HIV prevention, then they have to commit themselves to trying to take it on a regular basis.

The adherence literature is pretty clear that there are sort of two kinds of nonadherence we have to worry about. One is people often don't take the drugs as they're prescribed to them, so we tell them to take it every day, they say ah what the heck I'll take it every other day. But the other issue that's important for PrEP is the issue of persistence. And that is if you look at the literature for statins for example, almost 40% of patients have stopped taking their statins by four months after their first prescription. So I think since HIV exposure is going to be an ongoing issue for most people who're put PrEP, it's an issue both of getting them to take it daily and getting them to return for the scheduled visits, and getting them to stick with PrEP if they're good at taking their pills so that it has the best chance to protect them over the long run.

CHELSEA WHITE: Someone else posts the question, would you want to wait till he fully treated for syphilis until beginning PrEP?

DAWN SMITH: Absolutely not. You want to provide him with protection from the moment that you determine it's safe to begin PrEP. So once you've confirmed that he's negative, there's is no reason to defer his PrEP until he receives treatment for his STI.

KAREN HOOVER: I think Dawn has on one of her slides, that the drugs in PrEP do not interact with bacterial STI treatment drugs.

CHELSEA WHITE: Someone else asks, if someone stops taking PrEP, would they be eligible to go back on it at a later date?

DAWN SMITH: Absolutely. I think one of the ways that we've talked about PrEP, one of the examples we've given is, when you see young women and you start them on birth control pills, you don't expect that going to stay on the pill until they go into menopause continuously. As situations is their life change, they change their method of contraception. And we think the same thing will be true for PrEP. There will be some patients who are on it for a few months, some patients who are on it for a few years and some patients who are on it for longer periods of time.

But if for example somebody just to give an example, you know I have a positive partner and my partner is taking a job on the other side of the country, and is going to be away for a year

doing something else. I may decide I don't want to take PrEP during that year while my partners away and that makes perfect sense but then when he's coming back, I should be able to restart it, assuming that I'm HIV negative and that my renal function is normal. So absolutely we expect the people who stop it should be able to go back on it when it makes sense for them.

CHELSEA WHITE: Another question was put up. Am I, the person asked, Am I clear in understanding that viral suppression could mean discontinuation of PrEP for the uninfected partner.

DAWN SMITH: I think that's a strategy that's being tested in Africa and I think there the concern is that they are having trouble affording at the national level, all the drugs they need for the positive people and so they're trying to figure out what's the best strategy to provide both treatment and prevention. I think in the United States where that kind of financial trade off is not so much an issue, it's a matter of the clinician sitting down with a couple and talking about what they want to do. I think where the positive partner is not yet virally suppressed, a clinician might be more guy might promote PrEP more to the negative I think if the positive partner is suppressed and has been suppressed for awhile and has no STIs and as far as you know there are no outside partners, then it's a different conversation.

But again there may be some HIV negatives who want the added protection of PrEP just in case their partner has an unexpected viral blip. There may be other patients who feel really comfortable continuing condom use with their positive partner. So it is more of a judgment call and a kind of conversation with the couple, once the positive partner is virally suppressed.

CHELSEA WHITE: Someone else asked, so when someone wants to discontinue PrEP do they just stop immediately or are they weaned off the drug?

DAWN SMITH: No, they can stop immediately.

CHELSEA WHITE: Someone else asked, does PrEP affect someone on their birth control?

DR DAWN SMITH: No, there's no interaction between these drugs and contraceptives

CHELSEA WHITE: OK that is questions for now that I have received. I think I'll be able to advance the next slide. I'll try now so we can move on to the second case study.

KAREN HOOVER: OK so a 30-year-old black woman with a second episode of gonorrhea in the past year, tested negative for HIV three months ago, reports frequent partner change, she had three male partners in the past year, and she doesn't use condoms very often. So what would be, what would you do with this woman? Do you think she's a good PrEP candidate?

CHELSEA WHITE: Someone wrote yes.

KAREN HOOVER: Someone wrote yes we agree.

CHELSEA WHITE: Got a couple of yeses.

KAREN HOOVER: So she had negative HIV test three months ago. What do you think, do you think you would go ahead and start her on PrEP or would you want to retest her.

CHELSEA WHITE: Someone wrote Yes but, OK people are writing very quickly, people are saying retest and retest her retest her for HIV.

KAREN HOOVER: Excellent So what other would you want to do with her?

CHELSEA WHITE: Test for all STIs

KAREN HOOVER: Pardon me?

CHELSEA WHITE: Folks mentioned Test for all STIs as well as pregnancy, kidney function, Hep B perfect?

DAWN SMITH: You know I will add here, this hasn't been seen in women but it has been seen in MSM, and that is that they're at risk for sexual acquisition of Hep C. And so both for injection drug users and for MSM, it may be important to retest people for Hep C. I don't think sexual transmission has been seen as frequently in women.

KAREN HOOVER: That's right

DAWN SMITH: So you may not need to do that for this woman.

KAREN HOOVER: That's right. Yes sexual transmission of HIV is usually associated with traumatic tissue encounters, where there could be an exchange of blood or exposure to blood what did I say?

DAWN SMITH: HIV

KAREN HOOVER: HPV I'm sorry I misspoke. And so do you think you would recommend contraception for this woman?

CHELSEA WHITE: Yeah someone wrote encourage increased condom use.

KAREN HOOVER: Yeah and perhaps additional contraception. Dr Smith here is saying a long and I agree with her.

DAWN SMITH: A long acting contraceptive method.

KAREN HOOVER: Right of course unless she's trying to become pregnant. In which case then you would want to work with her and her partner to conceive without transmission if her partner is positive.

CHELSEA WHITE: Someone also suggested and may be assessed if she has issues with negotiating condom use.

KAREN HOOVER: Exactly. That's I think one of the really, one of the beauties of PrEP for women. It puts the either control in their hands [INAUDIBLE].

CHELSEA WHITE: Someone also suggested female condoms that's also an option.

KAREN HOOVER: OK

CHELSEA WHITE: OK would you like to move on to the next case study?

KAREN HOOVER: Sure OK so a 30-year-old woman presents with cellulitis at drug injection site and she's told you that she injects heroin and so we know that she found is a person who injects drugs. And she had a recent relapse from drug treatment, she was being treated with buprenorphine but had a relapse where she started injecting heroin again. She had an HIV test six months ago and it was negative. She injects with her main sexual partner and she doesn't know his status. She isn't aware of and we don't think there's any needle or syringe exchange program where she lives. And she also really doesn't use condoms very often. So what do you guys think? This is a female person who injects drugs, PWID. What would you do with her when she came into your office?

CHELSEA WHITE: Folks are saying HIV test. She and her partner needs to be tested, Hep C test, test for ACV and HIV test.

KAREN HOOVER: For both?

CHELSEA WHITE: Yep. Increase condom use or abstain until knowing status.

KAREN HOOVER: Yep

CHELSEA WHITE: Do not share. Drug treatment encouragement. STI test. [INAUDIBLE] HIV PrEP.

KAREN HOOVER: Perfect and so do any of you in the audience-- do any of you prescribe Suboxone for your patient populations?

CHELSEA WHITE: Someone also added pregnancy test to your earlier question [INAUDIBLE].

DAWN SMITH: The other thing that you could consider in that you know she's injecting with her partner, so in a primary care setting you should also be trying to engage her partner in care. Both for his injection drug use as well as for possible hepatitis or HIV infection where people have a main sexual partner, providing health care to both members of the partnership, doubles your chances of really making a difference in this sort of health outcome.

KAREN HOOVER: Right. And I think HIV prevention with PWID population, there are a lot of ways to prevent infection and any one method isn't perfect and fail proof. And so we know PrEP will likely be very effective. But if adherence is less than perfect, it may not be 100 percent. She doesn't have a syringe exchange in her city, but as your primary as her primary care provider you might want to explore if it's legal for her to buy clean syringes in her

pharmacy. Because often even in locations where there isn't a syringe exchange, access to clean needles can be acquired in that way. And so you were trying to offer as many HIV prevention modalities as is feasible, syringe exchange, PrEP and I think ultimately you want to get this person into treatment, because if you obviate her need to inject, you know with effective treatment then you really greatly reduce her risk of becoming infective.

CHELSEA WHITE: Someone also suggests to provide education on bleach kits?

KAREN HOOVER: Yes

DAWN SMITH: Absolutely

KAREN HOOVER: Yes absolutely its a harm reduction strategy that is, I think not a first choice you know using a clean syringe each and every time a person injects is what we would really like to see. But when that's not always available there are bleach kits and really great instructions where you can clean you're injecting equipment, and that helps.

CHELSEA WHITE: With all the feedback I received from the audience, was there any additional questions folks might have? You're more than welcome to post them now. OK We'll give another minute for folks to pose any additional questions they might have for our presenters? Someone wrote, compliance is always such a hurdle the data that they are working on a combination of combination Truvada with birth control and an IUD or [INAUDIBLE] is very exciting.

KAREN HOOVER: See I don't think there's any work ongoing for IUD imbedded PrEP agents Are you aware of any Dawn?

DAWN SMITH: There are studys where they're trying to embed them in cervical wombs, but I think again what we need to focus on right now is implementing what we already have. That's four or five years from now

KAREN HOOVER: Right.

DAWN SMITH: if it works out and gets FDA approval and then gets marketed. So I think all that's very exciting. In the meantime, we have to try to figure out how to use what we have to the best effect.

CHELSEA WHITE: Any other questions?

KAREN HOOVER: I just want to say I think that all the questions and comments in response to the case studies have really been excellent. I think the primary care providers in the audience should be reassured that I think you'd be great providers of PrEP. I think we're really delighted by your interest and your knowledge of PrEP.

CHELSEA WHITE: OK so I wanted to thank everyone for participating in today's webinar. We really appreciate both of our presenters for being on this webinar. We hope that the

information we were able to provide us was useful and does anyone have any final comments or questions at this time? All right, thank you all take care.