PRE-EXPOSURE PROPHYLAXIS

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Pre-exposure Prophylaxis
[video transcript]

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- [Rob] Good afternoon everyone. Thank you for attending today's This Month in HIV. Today we have Jeffrey Kwong who will be presenting on Pre-Exposure Prophylaxis or PrEP. We ask that everyone please maintain a muted line so that we get no background noise during the presentation. We'll leave about 10 minutes at the end for question and answers. If you have anything immediate please just type a question into the box and we can also address it later. After the program today we will be sending out the evaluation forms. Those will be your participant feedback form as well as your free CME/CNE credit for the hour. Please make sure that everyone fill these out since we are funded through the New York City Department of Health AIDS Institute we do need to turn these in to them to account for the programs that we do. Again my name is Robert Walsh. I am the program coordinator with Mount Sinai Institute for Advanced Medicine and the Clinical Education Initiative. Afterwards if you have any questions for me, you've been receiving emails from me and keep a lookout for next month's This Month in HIV. With that I'm going to turn it over to Dr. Kwong.

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- [Dr. Kwong] Great. Thank you very much Rob and good afternoon everybody. Thank you very much for joining us. Today or this afternoon we'll be talking about HIV Pre-Exposure Prophylaxis.

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I have no relevant disclosures.

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These are the objectives for this talk. I'm going to be reviewing and discussing the guidelines for Pre-Exposure Prophylaxis; describing the selection of candidates for PrEP; describing and discussing the management of patients on PrEP including spouse, PrEP therapy and side effects; discuss the challenges associated with PrEP and discuss follow up care including labs and counseling.

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So we start with this slide which is from the Centers for Disease Control which really is a very eloquent slide that shows us kind of the trends in the epidemic over the last 25 years or so. And we can see that we've made significant progress in terms of HIV treatment. You can see that since the introduction and availability of highly active anti-retroviral therapy in the mid 1990s, we’ve seen a significant decline in the number of deaths and the number of new AIDS cases over the past several years.

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However, in terms of new infections, particularly on a global scale we still have a lot of work to do. It's estimated that nearly 6000 new infections occur every day according to the World Health Organization which translates to about four new infections per minute on a global scale.
If we look closely at the trends in the US, we see here this is from the Centers for Disease Control as well. The last several years that in the majority of populations risk categories; heterosexuals, injection drug users, have been declining slowly. However, in men who have sex with men, MSM sexual contact remains the most common route of transmission of HIV in the United States. And according to this slide you can see the trends are actually increasing or were increasing through 2013 for this population.

There was a statement by the Institute of Medicine a couple of years ago that really speaks highly about the impact of prevention and one of the statements or quotes was that treatment costs for HIV are really unsustainable. Greater emphasis must be placed on preventing new infection.

Now in New York state we are actually doing quite well. This is some data that shows you the trends in New York state in terms of the number of new infections over the last several years. You can see in New York state unlike the general population, we've actually had a significant decline in the number of new infections which really speaks highly of the public health effort that we have here in New York state.

If we look again at the populations at risk and the proportion of new infections in New York State, this mimics very much the general US picture which shows that in most situations over the last several years MSM transmission still accounts for the highest proportion of new HIV infections in New York state between 2006 and 2013.

So I’m pretty sure many of you are familiar with the governor's plan to end AIDS by 2020 and as part of that plan this is really something that's quite avant garde and something that I think New York state should be very proud of. The three components include part three, which is providing access to Pre-Exposure Prophylaxis for high risk persons to keep them negative. And when we think of prevention and PrEP it's really important to remember that PrEP really exists within the context of other prevention tools that we have and that are available to us and that includes things like safer sex counseling, barrier protection, needle exchange, post exposure prophylaxis, both occupational and non-occupational post exposure prophylaxis, treatment and prevention and PrEP falls into one of those prevention tools.

Now in terms of the data that supports PrEP there have been many studies done in different populations including men who have sex with men, transgender women, heterosexual couples and injection drug users and you can see here beginning even with the Caprisa 004 back in 2008 or so there have been efficacy shown in all the trials. You can see highlighted in red the overall efficacy rates reported in the different trials for PrEP and the efficacy rates for PrEP using different forms of tenofovir or tenofovir emtricitabine have been quite successful anywhere from 39 to as high as, more recently reported in two trials, 86% and these two trials, the PROUD and the Ipergay trial were studies that
reported earlier this year and I'll be talking about the Ipergay trial in just a little bit but you can see that overall the efficacy rate for PrEP is quite high.

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Not all studies have been successful. There've actually been two trials that have been published and that have been reported on. The FEM-PrEP trial and the VOICE trial which looked at pre-exposure prophylaxis primarily in heterosexual women in Africa and in these two trials there was no benefit in tenofovir or tenofovir emtricitabine for pre-exposure prophylaxis. There've been many reasons or analysis regarding some of this. Some of this relates to cultural issues regarding stigma and access to healthcare services. But these two trials are the only two so far that have shown a negative or not favorable outcome for pre-exposure prophylaxis. But the majority of trials have all shown a favorable outcome.

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So beginning with the release of the iPreX trial which focused primarily on men who have sex with men and transgender women back in 2010 over just the last several years the CDC has issued interim guidance for different populations and then in 2014 issued a more formal clinical practice guideline. This is just a screenshot of the cover of that document. This is easily available on the internet which you can find under PrEP CDC guidelines. There's also a clinical supplement that is available for clinicians that provides additional information and tools for clinicians to use in their practice. The New York State AIDS Institute also has clinical guidelines or recommendations available on the New York State AIDS Institute website.

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But who is a candidate for PrEP? The guidelines outline three primary populations that would benefit from PrEP. Those include men who have sex with men, heterosexual women and men and injection drug users. Remember again PrEP should be used as just one prevention tool to reduce or minimize the risk of acquiring HIV infection. In particular people who might be good candidates for PrEP include people who've had a recent bacterial sexually transmitted infection, those who report having multiple or a high number of sex partners, those who report are having inconsistent condom use, those who engage in commercial sex work or those who report sharing injection drug using equipment.

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Now for people who may not be familiar with or not a lot of experience in terms of assessing risk, this is a tool the MSM Risk Index which is available through the CDC PrEP provider supplement. And this is just a set of questions, user standardized questions that you can go through with your client to see how they would score. You can see here the types of questions they ask regarding age, regarding if they've had sex with men, how many partners they've had unprotected receptive anal sex with, if they've used any other concurrent substances such as methamphetamine, crystal or speed. People get scores for these different risk factors and according to the algorithm, if somebody scores 10 or greater this would be somebody that would be a potential candidate for HIV prevention services including PrEP.
Some of the key points to remember when prescribing or offering pre-exposure prophylaxis is that one, PrEP should not be offered as a sole intervention. That it really should exist within the context of other prevention services. That individuals who report lack of consistent barrier protection that is not a contraindication for PrEP. That's actually probably a good indication for PrEP. This is the key thing I think. The most important of all them which is that clinicians should really wait to confirm that somebody is HIV negative or HIV uninfected prior to prescribing PrEP. That individual who may present with or be suspected of having acute HIV infection should be screened with HIV RNA testing or plasma viral load in addition to traditional fourth generation or third generation HIV assays. If somebody does become HIV positive that they should discontinue PrEP immediately, primarily because we know that PrEP is a two drug combination and those individuals with HIV infection actually need at least three drugs to treat HIV effectively.

There's only one medication that is approved for pre-exposure prophylaxis in the United States and that is tenofovir emtricitabine also known by the brand name of Truvada. They way that it is indicated for prescribing, the way that the guidelines recommend is for daily dosing and that is the only method that's approved and shown to be effective for PrEP in the majority of the studies and again I'll go over the Ipergay trial and event driven dosing in just a little bit. And that really the efficacy of PrEP was demonstrated with the context of other prevention and risk reduction services.

Absolute contraindications for PrEP include HIV infection and individuals who have a creatinine clearance less than 60. We know that tenofovir is renal toxic or it can affect renal function so again we need to be monitoring renal function closely and not prescribe it in individuals with a creatinine clearance less than 60.

Within the New York state guidelines there is a checklist for providers to assess patients before they go on PrEP and these are just great things to do with all of your patients and this can be done within the context of one visit or over the course of a couple of visits and it can be done with several different providers and I'll talk about that as well in just a bit. But some of the key things to do. Definitely screen for signs or symptoms of acute HIV infection and if that might have happened in the last six weeks. If they've had a high risk exposure you want to assess them to see if they're had any flu like illness, any pharyngitis adenopathy, non-pruritic maculopapular rash on the torso. Those are characteristics of acute HIV infection. To review any concomitant or concurrent medications especially if there are any potential renally toxic medications that may pose issues in terms of toxicity for the patient. Assessing mental health and substance use if they need referrals or assistance with any of those other issues it's important to provide appropriate referrals, making sure that they understand and truly know why they're taking PrEP and assessing their motivation for PrEP, especially their willingness and ability to adhere to take daily medication. The other interesting component or the one thing that comes up with PrEP and putting patients on pre-exposure prophylaxis is that they do need to be monitored quite
frequently, about every 90 days or every three months. So for people who may not necessarily be
engaged in primary care, it's a great way to get them engaged in primary care and to connect them to a
provider who monitor and follow them. Other issues to assess: Definitely screen for domestic violence,
assess for housing issues, do they have means to pay for PrEP. I'll talk a bit about that towards the end
as well. And then if a couple that's potential considering having a child or using PrEP for pregnancy
issues, just evaluating their fertility goals and talking about some of the potential risk associated with
PrEP and pregnancy.

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In terms of laboratory evaluation, it's quite straightforward so the key thing is making sure the individual
has a negative HIV baseline test either using a third or most places now are converting to using fourth
generation antigen antibody assays. Again if somebody is suspected of having a recent exposure, doing
or adding on a plasma viral load would be an important component of that. So all the patients that I see
for PrEP- and I have a fairly large PrEP panel in my own clinical practice- that is one of the questions I ask
typically, which is tell me when was your last unprotected or last sexual exposure, and that will just help
me determine which antigen antibody test or if I need to add on a viral load test at that time. So that's
just a key question to remember for when assessing and doing your baseline evaluation with your
patient. Other laboratory analyses that should be done and performed include a basic metabolic panel
primarily to assess renal function, urinalysis to assess for any existing or preexisting proteinuria,
serologies for hepatitis A, B and C. For many of you out there you probably already know that tenofovir
and emtricitabine can be used for patients with chronic hepatitis B so if they have chronic hepatitis B
and you put them on tenofovir emtricitabine, that should address their hepatitis B. However, if you have
to take them off of tenofovir emtricitabine for any reason and they have chronic hepatitis B, do know
that you should replace agent that's active against hepatitis B in the regiment because patients are at
risk for having hepatic flares if they have chronic hepatitis B and you discontinue tenofovir emtricitabine
unexpectedly. Screening for sexually transmitted infections, including extra-genital sites both for general
and rectal GC and CT testing is appropriate for individuals who report having any oral or rectal sex. Also
screening for syphilis and or people who are of child bearing potential doing a pregnancy test as well.

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According to the guidelines the recommendation is to do an initial supply of about 30 days of tenofovir
emtricitabine to see if the individual tolerates it, to assess their adherence. And then if they do well after
the first 30 days you can renew the prescription for a total of 90 days. It is recommended not to do more
than 90 days at a time. Sometime these are issues that are bound by the pharmaceutical companies and
somebody's insurance carrier only allows them a 90-day supply not a 30-day supply. So, again a case by
case basis I have to do different things for different people. Some people can get it filled their
prescriptions as a local pharmacy, some people require having their medications sent directly to a mail
order pharmacy. So those are things that you have to again evaluate on a case by case basis, but again
the maximum is a 90-day supply with zero additional refills. For people who again who have chronic
hepatitis B just remember that tenofovir emtricitabine is active against hepatitis B. And then the other
thing that you want to do for somebody before they begin treatment is to provide ongoing risk
reduction counseling, and discussion of other barrier methods as well.
In terms of medication adherence and counseling, these are just some key points here in terms of medication interaction counseling. It's the same types of counseling we would do with somebody who is starting treatment for HIV infection. Definitely try to identify barriers to adherence. If somebody reports issues where they are missing doses consistently, more than once a month, definitely try to assess and see if there are ways to help increase their adherence either through incorporating it into a daily routine, giving them a pill box, having them set an alarm reminder, getting other friends who are supports involved in reminding them to take their medication. So all of those key adherence tricks and tools of the trade that we've used for our HIV patients definitely translates to our pre-exposure prophylaxis patients as well.

Other key things that I think many of us do already but just to re-emphasize, especially when talking about pre-exposure prophylaxis or any sort of potential risk issues, it's important that providers offer and create a trusting and confidential environment with their patient, making sure that you're able to have an ongoing dialogue with your patient, that they're able to accurately report to you their risk, and then if they do report ongoing risk to really have the opportunity to strategize with them on ways to reduce their risk in the future. Remember to always just reinforce that it's consistent use of PrEP together with other prevention methods offer the highest level of protection.

Now we talk about daily adherence to PrEP. There is a little bit of wiggle room here in terms of pharmacokinetics. This is a graph from a study that was published from the iPreX open label extension study or iPreX OLE and in this analysis what they did was they looked at the pharmacologic concentrations needed in order to provide adequate protection. So they found actually four doses at a minimum per week were similar to seven days in terms of providing the same amount of coverage or protection. So in reality most people if they take it about four days a week will probably get the same benefit as if they take it seven days a week but I always tell my patients to take it seven days a week just in case they miss a dose here or there they're at least protected if they only four days a week and they miss a dose here or there then they fall below the therapeutic range of protection and so they run the greater risk of not having full benefit of pre-exposure prophylaxis.

That being said, there was a trial and probably many of you might have seen this or heard about this. Actually the first person that told me about this was from a patient of mine who sent me an email at two in the morning when the results of the Ipergay trial were first announced. And this was a trial that was done looking at what was called event driven dosing. So in this trial, this was a trial looking at high risk individuals and what they did they were instructed to take two doses of PrEP prior to exposure, two to 24 hours prior. One dose of PrEP on the day of exposure and for every day after and then one day following the last exposure. In this trial they actually found that there was an 86% reduction in people who were using the event driven model compared to placebo. However, if you look at the average number of doses people were taking, they were taking about four doses per week which again in the
previous slide showed that four doses and seven doses a week are comparable in terms of efficacy. So even though this study is just a small study of slightly less than 400 individuals, this may show evidence for future directions for PrEP. But right now really daily dosing is the only option that is recommended.

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In another study that was just reported over the summer at the International AIDS Society Conference there was another study looking at time driven PrEP and event driven PrEP. This is more of a feasibility study rather than an efficacy study. This is done both in Harlem, Bangkok and then also in Africa in women and Bangkok and Harlem cohorts for primarily MSM and transgender women. In this trial people were randomized to one of three arcs; either a daily PrEP option, a time driven PrEP option where they did one dose twice a week and then one dose following a sexual encounter or they did an event driven model where they did one dose before and one dose after sex and they were evaluated over a period of about six months.

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And they actually found out just in terms of feasibility again not efficacy but just in terms of adherence and looking at the overall structure, that higher adherence rates were associated with people that took the medication daily versus those who did a time driven schedule or the event driven schedule. So again this speaks to the benefit of keeping things on a daily basis just in terms of making sure patients adhere to the correct dosing strategy.

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In another trial that was published or presented earlier this year, this is from the Adolescent Trials Network. This looked at younger men who have sex with men 18-22. It's a small cohort about 200 individuals and in this trial people were all received a behavioral intervention. One of the standardize behavioral interventions that have been developed and are more evidence based, and they were provided pre-exposure prophylaxis and also monitored over time. In this trial it was primarily young black men although you can see the ethnic and racial breakdown listed here. There were four seroconversions overall and throughout the study and people who seroconverted had no detectable tenofovir drug levels. So that just speaks to the importance of adherence and the key thing here, the other interesting thing was that there was no drug resistance detected in people who seroconverted.

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But you can see over time the slip in adherence across different racial ethnic groups and you can see that in many of the groups the adherence decreased over time over the study and so kind of the key message here, things that we've learned before from other studies is that maybe some of our adherence issues and some of our counseling and educational messages for younger men who have sex with men may need to be more intensified or adjusted to meet their particular life needs and adherence needs. But in general for everybody, the follow up monitoring is listed here. So every three months people should get follow up HIV testing, you should assess their medication adherence, look at and assess for any adverse events and screen and assess for any sexually transmitted infection symptoms that they may have. Every three months and then you can do it every six months thereafter, you want to assess
renal function just to make sure that their creatinine clearance is stable, and then the guidelines recommend at least every six months testing for bacterial STIs- again that is just in general. So for some of my patients that I see, many of them report every three months having multiple sexual partners, so I typically will screen every three months for my patients. The patients where I don’t screen every three months typically are those who are serodiscordant or serodifferent couples, where they are sexually exclusive and sexually monogamous- someone they’re not having outside partners. I might not necessarily screen them for STIs every six or every three months, but I might do it periodically. Then at every visit, it says at least once a year, every 12 months, evaluate the need for ongoing PrEP. So definitely in my clinical practice, I’ve seen individuals who have used PrEP for higher risk periods in their life and their situation changes; either they get into a sexually exclusive, sexually monogamous relationship or they are just not having as much sex as they used to and so they don’t necessarily want to take a medication every day for something that does not occur that frequently or for a situation that is considered relatively low risk or no risk, and so for those individuals we can stop PrEP. I always tell patients that if your situation changes, or your relationship changes definitely you can go back on PrEP. The only thing that we need to do before we get you back on PrEP is to ensure that you are HIV negative and to go through the baseline testing one more time.

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Another use of PrEP is for couples are trying to conceive in serodiscordant situations. So the current clinical guidelines say that PrEP should be discussed as one of several options to protect the uninfected partner during conception and pregnancy.

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And if we are looking at the guidelines again you can see that if somebody becomes pregnant on PrEP, it's just important to let them know that there aren’t a lot of studies or outcome data on PrEP during pregnancy but we do know that in our HIV positive mothers, that many of them do use tenofovir emtricitabine before and during pregnancy and so in those situations there are no major issues in terms of outcomes. But anybody that is thinking about getting pregnant should be informed of the lack of data that surrounds the use of PrEP during conception and pregnancy, and all pregnancies should be reported to the anti-retroviral pregnancy registry.

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Just like PrEP is one tool in the HIV prevention toolbox do know that PrEP is one tool to use in the conception toolbox. So other ways that couples can utilize to help reduce their risk of infection during periods of trying to conceive include things like treatment as prevention that’s when we treat a partner with HIV to fully suppressive level. Using PrEP continuously, using condoms and PrEP and then no condom during the fertile period, or things such as sperm washing and in vitro or intrauterine fertilization or other methods to help reduce the risk of HIV transmission or infection during conception.

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If we look back at PrEP and the FDA approval of PrEP as an intervention. I think before PrEP was ready to be unveiled we thought there would be a huge huge uptake of PrEP that people would be knocking
down the doors coming to providers and insurance companies were thinking about it and other health systems were thinking about how to implement PrEP. But in reality the initial uptake for PrEP was relatively low. This is data from Gilead Sciences that showed during the first year and a half after PrEP was FDA approved, that there were only about 2000 prescriptions written in the United States in total. So really not a huge uptake after it was first approved. Interestingly enough, during the first year and a half about half of the prescriptions were among women so that's great in terms of getting access to a population that was definitely at risk. Many of the prescriptions for women were in the southeastern part of the United States where we know that heterosexual transmission is quite high.

So when we think about PrEP what are the barriers to PrEP uptake and PrEP implementation?

And there are really two types of barriers or levels of obstacles that we can think of. So there are user level barriers and provider level barriers. Some of the user level barriers include just the lack of knowledge or people not knowing that this is an intervention that is available to them. People who are uninsured or unable to pay for PrEP- in New York state we're very fortunate; I'll talk about that again in just a bit- there's issues about concern about disclosure and stigma. So some people may fear that they're taking a medication that's known for treating HIV, that somebody may mistakenly assume that they have HIV when they don't have HIV. There's also the issue of stigma regarding risk compensation. So there is the stigma that people who take PrEP want to engage in condomless sex and therefore may be more sexually promiscuous or may be not as focused on using condoms as a prevention method and so there's that whole stigma that surrounds that issue that plays a barrier in terms of the patient or user level perspective. From the provider level barriers there are issues in terms of just providers are unaware of how to provide PrEP, how to write for it, how to do the follow-up. As you can see hopefully I've outlined that it is quite straightforward and actually the complexity is not that difficult for the majority of patients. People may have discomfort or clinicians may have some discomfort regarding assessing candidacy, in talking about sex, or talking about drug use with their patients and so some of these other issues provide obstacles or barriers for PrEP implementation for many people.

But I definitely think over the last year or so definitely here in New York City and in my clinical practice the demand for PrEP is increasing significantly and I should caveat that with the fact that my clinical practice is located in Chelsea and so many individuals within the neighborhood are on PrEP and many people get referred to me or come in through word of mouth and so in a typical day of 20 patients 773 about half of my patients either come see me for PrEP initiation, PrEP questions or PrEP follow-up. So definitely that has changed the scope of my practice quite a bit.

There are also social media sites that are available. There's a Facebook page that's got over 10,000 users as well that really talk and publicize the availability of PrEP from the consumer perspective and so
definitely I think as time goes on more and more of us as providers or clinicians will encounter patients who are interested in PrEP or who want to be on PrEP.

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So other factors that play into accessing or implementing PrEP to its fullest.

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So in terms of provider level factors, some studies have suggested that providers just are kind of slow sometimes in terms of adopting new interventions. If it's something that's a new indication many providers there's just a time delay in terms of people feeling comfortable with providing medications or providing an intervention, especially if you aren't familiar with prescribing anti-retrovirals. The whole concept of providing HIV medications to somebody who's not HIV infected can be very daunting or it can be scary for some individuals. But do know there is a lot of support available. There is a reference at the end that I'll share with you as well. And there's also system level factors.

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In terms of some analysis this is just a survey or analysis that was published last year that looked at infectious disease physicians within the Infectious Disease Society of America, and of their membership most of them supported the use or the idea of pre-exposure prophylaxis however only a small percentage, less than 10% actually have the opportunity to provide PrEP. And some of the reasoning behind why there was such a discrepancy between this was that many people thought because they were an infection disease specialist or HIV specialist that they were located in an HIV clinic and maybe providers, sorry, consumers or patients who were interested in PrEP probably felt intimidated or did not want to go to an HIV provider if they did not have HIV. And so the people who have the most knowledge and most experience with providing PrEP or prescribing tenofovir emtricitabine may not have been able to access the patient population at risk. And so this really kind of speaks a little bit to the role of primary care providers and non HIV specialists in providing pre-exposure prophylaxis, at least as an entry way or gateway to getting people connected to providers who are able to provide PrEP.

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Other issues that providers have expressed include issues regarding the cost of the medications, concerns about drug resistance, concerns about starting a medication that is toxic in patients who are otherwise healthy, concerns about efficacy of real world PrEP and people who thought it might be too time consuming.

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This is another analysis or survey that was done with members of the American Academy of HIV Medicine. And again similar concerns were reported here in terms of physician attitudes here, that people thought that PrEP would lead to the development of drug resistance, that it would lead to increased risk behavior taking and also in terms of compliance and adherence were other concerns.
Now in terms of drug resistance, I reported earlier from the other trial from the Adolescence Trial Network that in their study, there were no resistance in people who seroconverted while on study, and this is a chart this is from the iPreX trial. This is the large trial of MSM that was published in 2010 and in this trial you can see here the table was divided into two, infected and uninfected. Now in the iPreX trial, the people who fall into these two categories here actually screened at baseline as negative but were actually acutely HIV infected. So when they started treatment they were actually already HIV infected and in those individuals, there were some drug resistance mutations that developed. Again these were people who were infected prior to actually intervention. People who screened negative at baseline and were truly uninfected at baseline, who later seroconverted, you can see here that in both placebo and the intervention that there was no evidence of drug resistance mutations identified in that population.

In terms of risk compensation, that's why people engage in higher risk or in potentially not using condoms if they're on PrEP. You can see in the iPrEx trial that actually both in the intervention group and in the placebo group, that people who reported using condoms actually increased over time, over the course of the study. Now it's important to remember that in this trial people had access to ongoing counseling and risk reduction services on a fairly regular basis and so the level of counseling and prevention services was quite high in the study setting may not necessarily be the same in the real world study. So what does it look like in the real world?

Well I'll share with you a couple of other studies that were reported just recently. So this is a report from the PrEP Demo study that was done. This is information from three clinics in San Francisco, Miami and Washington, DC. This was just reported over this past summer at IAS and they found here in terms of overall retention in the trial that it decreased slightly over the course of the 12 months. That only about 63% of people actually had protective levels of tenofovir in their blood so meaning that they had, that they were taking it at least four to seven days a week to provide the efficacy needed to prevent HIV infection. So only about two thirds of the participants had enough blood level, so it speaks to a little bit more about the importance of adherence and counseling your patients about taking medications on a regular basis.

In terms of the risk compensation issue, this is a slide which was presented looking at the STI positivity rates over time, and you can see here at baseline and then at six months it actually declined over time. But then after six months the STI rates increased, suggesting that people might be engaging in more condomless sex over time. However, do know that the 48 week follow up data really is not that much different from baseline so it didn't not necessarily increase risk taking behavior but stayed relatively constant over time at least in the San Francisco trial the PrEP Demo study.
Now, slightly converse sphere was the Kaiser Permanente study that was published earlier this year as well. And this looked at STI rates in their cohort and you can see in red is the 12-month data, in blue is the 6-month data. And so you can see over time, actually in the Kaiser cohort there was an increase in STIs overall, including rectal STIs. Gonorrhea, chlamydia increased over time at the 12-month mark compared to the 6-month mark, suggesting that potentially risk compensation people not using condoms increased over time. However interestingly enough there were no new infections in this cohort. So that speaks to again potentially the benefit of PrEP in a real world study.

Other issues in terms of provider level barriers. This is just a survey that was published looking at provider knowledge about PrEP, and people who scored better on the study were people who had more experience with HIV. The recommendation was that maybe PrEP should be done or provided in collaboration with somebody with some HIV experience.

This is just an example. This was posted on the Facebook site for PrEP users and you can see here this is an actual prescription that was writing by somebody, I won't say where. But somebody had gone to the provider asked for PrEP, their provider said sure I'll write you one and this is what they wrote. So PrEP HIV as directed. That is not how we do it. I know everybody on this call already knows how to do it. One tablet daily, 32 refills right. Tenofovir emtricitabine is the drug. A prescription like this is not correct. So you can see that even though there might be providers who are interested in providing PrEP, making sure that you are knowledgeable on how to provide PrEP and to provide follow up is so critical in making sure that this is an effective intervention.

In terms of coverage and access, so most insurance carriers do provide coverage for pre-exposure prophylaxis; most of them do require a prior authorization. For patients who are under insured or uninsured there is an assistance program that is offered through the manufacturer of the medication. People do need to meet certain income requirements. Medications typically shipped to the provider’s office. So there's a little coordination that needs to be taken between the patient, the pharmacy, and the provider.

In New York State we're very fortunate to have support from the state in terms of providing access to pre-exposure prophylaxis so there is something called the PrEP-AP program or the PrEP assistance program. This is very similar to the AID AP program. This is just a screenshot of the website that's available. You can call here. This provides coverage for other supplemental things, such as STI testing, etc. Things that are required to provide PrEP. It doesn't not cover or provide medications, but it does provide coverage for ancillary services.
In terms of billing and coding these are the Z codes. Again many of you have just converted to the ICD 10 coding. These are the ones that I’ve been using basically for the last several weeks since the conversion. So Z20.2 which is contact with or suspected exposure to infections with predominately sexual mode of transmission or Z20.6. I’ve no issues in terms of reimbursement or billing or coding at this point based on these codes.

However, if you're considering implementing a PrEP program in your clinical setting, it's really important to look at both capacity and looking at systems level issues- some of them are listed here. And really making sure you have complete buy in from the entire organization so that people can have a good experience in terms of getting access and providing the services and getting the services that they need in terms of pre-exposure prophylaxis.

So know that there are clinical guidelines that outline the different things that need to be done including follow up testing, counseling, STI screening, mental health and substance use services etc.

As I said for some people or for some institutions, this is a great opportunity to consider team based approaches- so partnering or utilizing other members of your team such as social workers, HIV counseling and testing workers, patient navigators, pharmacists. You can do a team based approach, so that you can provide the full comprehensive list of services and go through the full recommendation of requirements for pre-exposure prophylaxis, utilizing all members of your team so you can provide adequate services and making sure that your organization has the appropriate capacity. In my clinical practice I don’t have a lot of extra ancillary support so it is possible for me to do it. I have somebody who does all the prior authorizations for me so it can be as very simple as that. Or other larger medical institutions have the social worker and a nurse and the provider so they have the three-member team. Whatever your organization has, whatever works best for you, I think it's important to consider and definitely make sure that you allow everybody to participate to help share the burden.

But again in terms of prevention other things to remember that PrEP is just one tool and I just also want to remind people about the use of other barrier methods but also non occupational post exposure prophylaxis.

This is sort of I think fallen to the shadows of PrEP. But do remember that this is an intervention that is available that may be appropriate for some individuals who may not have ongoing consistent risk, but who may be at high risk for certain periods. So non occupational or nPEP is an intervention used to minimize the risk of infection following a high risk exposure. It should be administered within 36 hours after exposure, ideally as soon as possible and the duration of treatment is 28 days.
On the New York State AIDS Institute webpage there are guidelines recommendations on how to provide non occupational post exposure prophylaxis. The recommended regimen is tenofovir emtricitabine with an integrate spaced inhibitor, so it can either be raltegravir twice a day or dolutegravir once a day.

Baseline and follow-up testing for individuals on nPEP include HIV testing, GC/CT and syphilis testing as well as testing for hepatitis B and C.

Now we've talked about Truvada and PrEP as the intervention but this is just a snapshot of the different types of PrEP that's being studied and investigated. So other forms of PrEP that are currently under investigation include; long acting medication formulations, injectable formulations, vaginal ring and other things are gonna definitely come down the pipeline. So I think as the future (static interference) we will see (static interference) PrEP available to us in the very near future.

This is just a map showing you the different study sites across the United States involved in pre-exposure prophylaxis trials or study.

And we talk about the end of the epidemic and really it's a combination of not just PrEP or biomedical prevention but it really involves all different things including testing, treatment, making sure that policy and resources are available, and behavioral interventions, all of these need to work synergistically in order for us to achieve our goal of ending the epidemic by 2020.

These are a couple of guidelines and webpages for your reference.

So some key points here. As consumer awareness of PrEP increases, providers should be prepared to offer accurate information and/or referral to appropriate expertise. Providers should continue to assess candidates for PrEP and offer it if appropriate. Organizations offering PrEP should assess capacity and consider the use of team based care.

For people who have clinical questions this is a clinical education line that's sponsored by CEI or the Clinical Education Initiative. This will provide you access to individuals or clinical experts who can provide consultation on specific cases for you. I encourage you to use this number or to visit the website for additional information.
And with that I will close and I think I've left about 10 minutes for questions.

- [Rob] Hi Jeffrey this is Rob, thanks. I do see that it looks like Wendy Ramsey asked a question but I don't see it. Wendy would you care to ask Dr. Kwong your question? Here we go Matt, no that's not it. I don't seem to see the question though that was asked. Oh hang on. I can hear you but- Alright, we have one from Dennis Kelly. When after starting trap is it effective? O crap it says. (multiple people speaking)

- [Dr. Kwong] Just in terms though the question about how soon after starting-

- [Rob] When after starting PrEP is it effective, yes.

- [Dr. Kwong] Yeah so the CDC guidelines at minimum seven days in order to get levels I posted to you. Particularly it takes for in a vessel protected level up to 20 days, 21 days or three weeks. So, I typically will tell patients not to have unprotected anal sex for at least seven days while on it, so that is really part of the key counseling message. Somebody for PrEP is to tell them the day they get their blood drawn at the lab until you give them the approval to start PrEP and at least, at least a minimum of a week after they've been on it that they should not have any unprotected or potential exposures to HIV or any high risk exposures period during that time just to make sure that they have adequate levels of drug.

- [Rob] Okay, Dennis Kelly has a follow-up question then I wanna ask Terry Hamilton's. How can this be effective when taken episodically for encounter?

- [Dr. Kwong] So I assume you're talking about the Ipergay trial. So the Ipergay trial which was the event driven dosing thing. So again remember in that trial people were taking it on average four times a week. Through four times a week it was the minimum amount of drug required to provide efficacy. So in the other trials such as the Adept trial, where they're looking at the different forms of event driven or time driven dosing they didn't not look at efficacy, they were really looking for primarily feasibility of this as an intervention. So right now we can't say that doing it sporadically or event driven is an effective intervention. It's still under investigation and daily use is the only funded way to counsel patients.

- [Rob] Okay, alright Jeffrey so we have a two part question from Terry Hamilton. Who specifically can prescribe PrEP, and how do you handle young people say aged 16 or 17?
[Dr. Kwong] So who can prescribe PrEP, technically anybody who has prescriptive privileges that would be a physician, physician assistant, nurse practitioner can provide or prescribe PrEP. Obviously it has to be within the confines of the individual's comfort level and if they feel skilled enough to provide that is probably one of the key criteria that people feel comfortable in prescribing it. But technically anybody who is a licensed prescriber in the state of New York, physician, physician assistant, nurse practitioner can prescribe PrEP. In terms of individuals who are under 18, so that is a tricky situation because the guidelines and the studies all required people to be 18 years or older. For people who are under 18 and high risk (interference) adolescent or high risk adolescent but at this point it's not FDA approved for that population.

[Rob] Next question is from Debbie Cusack. The Gilead data sheet advises patients not to take more than one pill at a time. What are the risks of use of more than one pill a day and follow-up to that, is any treatment required?

[Dr. Kwong] Sure so in terms of double dosing or maybe inadvertently or occasional inadvertently taking more than one a day, to my knowledge there are no major life threatening adverse events that occur with the occasional double dose on a day. So if they do double dose then on one day I would just have them assume their regular schedule the following day. They don't need to necessarily second day. And if you recall in the Ipergay trial people did take within a 24-hour period. So even though it says on the Gilead thing and it is in the prescribing instructions that it should be one pill a day, if people inadvertently take a second one during the day because they forgot, they weren't sure, you don't really need to do too much monitoring. You could check the renal function if you're concerned about it but if they have normal renal function and they're otherwise healthy then double dosing on one day should not make a huge difference.

[Rob] Okay Jeffrey, Dennis Kelly had another follow-up question that might need clarification. How can event driven Rx be considered if it takes seven days for drug level to reach efficacy.

[Dr. Kwong] Right so again in the Ipergay trial. It's the trial that's under investigation, not approved to use. But in those trials, so people were using it consistently throughout the course of the study so it wasn't just the first week. They were taking it fairly consistently over time so because they ended up taking four doses a week, they were able to achieve at least enough drug level over time. So I don't know if I'm answering your question correctly or if I'm getting to the point alluding to but if they were ongoing risk and they were taking it consistently for four days a week they had enough drug level in them to provide protection. So it's not like they were doing two doses and then having three weeks in between for a wash out and then doing it again. They were doing it fairly consistently every week and so
that consistency provides enough drug level. Does that make sense? It's hard when I don’t get to see you.

00:57:09

- [Rob] Are there any other questions from the group? Okay Wendy Ramsey. I was just wondering about the second study where it showed longer term the STI rate went up. Was it similar to the initial study though where if you compared it to initial rates there was no substantial increase along with the taking of pills daily?

00:57:41

- [Dr. Kwong] So in terms of the Kaiser Permanente study which shows a larger increase over time, so that one showed higher rates of STI suggesting potentially higher risk compensation activity there. But in the other trials they kind of balanced out from the baseline so in the Kaiser Permanente study they—Sorry, can you repeat the second part of the question?

00:58:17

- [Rob] Was it similar to the initial study though where if you compared it to initial rates there was no substantial increase, also with the taking of pills every day they have. Wondered if considered packaging like a BC pill.

00:58:33

- [Dr. Kwong] Oh so I think in the Kaiser Permanente study there was a slight increase in the rates more so than the other trial. And in terms of doing packaging or blister packing or doing other things to increase adherence, I think there are pharmacies that do a blister packs and can help people that are available. So I think that would be a great idea for somebody who's (interference)

00:59:15

- [Rob] Jeffery you still there?

00:59:17

- [Dr. Kwong] Yes

00:59:17

- [Rob] Oh okay. Thank you Wendy for those questions. I did just wanna address Tanya briefly. Tanya wanted to know if we'll be providing this presentation and possibly some of the Q and A in a follow up email. Some of the discussion is apparently being missed when opening up the microphone. Tanya the presentation is being recorded. Eventually it will be up on the CEI website for you to listen to again or view. What you can also do is if you wish to send a question to me for Dr. Kwong, I can forward it on to him. I want to thank everyone again for attending. Just to refresh everyone we will be sending a follow-up email with a regard to evaluations and your CME/CNEs. Just remember that we are funded through the New York State Department of Health so we would like that everyone please make sure to fill out your evaluations. It will not take long. And look forward to seeing you next month for This Month in HIV.

[Video End]