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ECHO: PREP FOR DRUG USER HEALTH

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[video transcript]

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Dr. Antonio Urbina, he is the medical director for the Mount Sinai Institute for Advanced medicine Seventh Avenue clinic in the city in New York. He also serves as medical director for CEI's HIV Primary Care and Prevention Center of Excellence. He has directed more than 10 HIV clinical trials and is a member of the New York State Department of Health AIDS Institute clinical guidelines committee. From 2007 to 2009. He served on the Presidential Advisory Council on HIV AIDS, and from 2014 to 2015. He served on Governor Cuomo's Task Force to end the AIDS epidemic here in New York State. Dr. Urbina. I will hand things over to you from here. Great.

00:49
Thank you, Lauren, and Linda and Jeffrey, for the invitation to speak. So I'm going to give an overview of pre-exposure prophylaxis, specifically how it relates to Drug User Health. And before I start, I'm going to list my disclosures. So I'm on the scientific advisory panel of Gilead Merck and ViiV. So our learning objectives today, we're going to discuss the New York State Department of Health AIDS Institute, clinical guidelines for PrEP on to prevent HIV and promote sexual health, review the surveillance data supporting PrEP use among people who use drugs and then describe really, I think, most importantly, kind of the role of long-acting injectables for PrEP in persons that use drugs. Okay, so we'll start off just one polling question. There's only one so okay. So which statement is true daily dosing of PrEP is the preferred dosing for people who inject drugs. On Demand dosing of TDF FTC has been shown to be an effective strategy for anal and vaginal, sexual exposure to HIV. Same day, rapid initiation of PrEP is not safe prior to receiving lab results. And if a patient misses their quarterly HIV testing PrEP, you should be held into an HIV negative status can be confirmed. So if they miss their follow up appointment, should you interrupt PrEP? So I'm just going to move it forward. But and we'll talk about some of these. But it's Yeah, so really, for persons that inject drugs, really the only datasets that are available are for TDF or tenofovir, disoproxil fumarate. Actually, in the tides study, they used monotherapy with TDF. Not to say that TAF FTC, that's DESCOVY is not effective, or even the long acting, PEP raltegravire is not effective. It's just there's no data. And we'll delve into that a little bit more. Now there is data that may be coming with long-acting cab and those that inject drugs. But for now, really, it's daily dosing of TD of the TDF FTC version that is preferred for those who inject drugs. Okay, so what are some of the PrEP options in the United States, and again, really want to discuss pre-exposure prophylaxis with all sexually active adults, adolescents, and offer PrEP to individuals who are at substantial risk of HIV acquisition. So for oral PrEP, these are kind of de scale. This is FTC TDF. And this is FTC TAF. And those are the two oral PrEP versions approved for Pre-Exposure Prophylaxis. And now we have the new game in town, injectable Apotek. Revere. All right, so let me just talk about some of the differences between the oral PrEP and why you would choose one, maybe over the other and I think the big

overlying region is FTC. TDF is now generic. So we're talking dollars, you know, for a month's supply, versus FTC TAF, which I think is like $1,300. So it's a big difference between FTC TDF which is now generic and FTC TAF. So really the go to and I'm fine with it as FTC TDF. It's also been the most studied in multiple populations. It does have issues with maybe small decreases in in renal function and bone mineral densities. But the big driver is the generic is available, and it has been studied and shown to be efficacious. In men who have sex with men, transgender women, heterosexual, and in persons who inject drugs. Now you'll notice that the efficacy drops a little bit in persons who inject drugs. And that's a little bit more you can imagine, imagine the inoculum from blood via a syringe, and that the barrier to protection is just a little higher. And then moving over to FTC TAF, it's effective in MSM and transgendered women only really, we don't have data for vaginal exposures. We don't have data for injection drug use, and the generic is not available. It's more friendly. From a renal standpoint, it's more friendly from a BMD bone, mineral density, Dan standpoint, it may be less lipid friendly than FTC TDF. And it may be associated with a little bit more weight gain. Okay, and then here we go. This is the money graph. Okay. So here we have the different populations, different types of sexual exposures, and then the recommendations for each of the agents. All right, so as you'll see that for oral FTC, TDF, really, it's got the broadest indication, so cisgendered men and women for insertive receptive and injection drug use, same for transgendered women and for transgendered men. Oral FTC TDF is also indicated also as an indication for on demand. And we'll go over that that's 211. So two tablets two to 24 hours before an exposure than 124 hours later, and then another 48 hours after. But that is really only indicated. For cisgendered men and women and for cisgendered. Men and women it's for insertive sex and receptive anal sex. So again, not for vaginal exposures or receptive vaginal sex. Oral TAF does not have an indication for on demand, it hasn't been studied, they are doing data, there is a study that will be looking on it. So it's really only indicated for insertive sex and for receptive, anal, insistent are men and women also for transgendered women. And for transgendered men, just receptive anal sex, we don't really have data on receptive sex with the Neo vaginas on and then Capitec Revere, I would say, it's the most broad, and the only indication that we don't have is really for injection drug use. Now, this is the caveat is that if someone were an injection drug user, I would say in particular, really not sharing using, you know, safe injecting, injecting practices. And if they also state that they have a sexual risk for HIV, then one can prescribe. I am Capitec Revere, and we'll go over kind of like but I would say if somebody really gives us a risk factor injection drug use, you may want to lean more towards oral daily FTC TDF. Okay, so this is kind of Tegra Veer. Kavin Tegra. Vir is for adults and adolescents at least 35 kilograms have to make sure they're really negative before you start. So more a viral load and a fourth-generation test. Within a week of that first injection, I'm really screened them for signs and symptoms of acute HIV infection and no contract indicated medications which are really few All right, so really the data Oh, eight three and oh eight four looked at long acting injectable Peppa Tegra, Vir for PrEP and looked at two populations so Oh, eight three was men of sex men with men who have sex with men and transgender women and oh eight four was in a cisgendered women. The study designs were

similar they were double blind double dummy. They started off with this oral cabinet Tegra veer leading, and then they randomized them to either injectable cap or daily oral FTC TDF. And then they had this kind of like extension phase. And again, in this data, now, this is the unblinded all data. What we found was statistically significantly few Were HIV infections in those that were randomized to the injectable arm versus oral. And this was in both study populations. And the real driver of the difference was adherence. So as with any oral medication that should be taken daily is that there are adherence lapses. And at least in this study, there was no lapses with adherence to the injection visits. And that's something that you also need to have a shared decision with the patients Hey, listen, these are our options for PrEP. If you do choose the injectable, yes, you won't have to be concerned with taking a pill for two months, however, you do need to come to your injection visit.

10:45
So it's important really to have that information out there and upfront. Okay, so one of the advantages, I think, to these long acting is that they don't cause decreases in bone mineral density. So this is a study the OA three study embedded where they looked at DEXA scans and they looked at bone mineral densities, and they compared the long-acting cabinet Tegra Vir to oral FTC TDF. And basically what you saw was that the long-acting cabinet Tegra Vir were associated with statistically significant increases in bone mineral densities, compared with decreases and FTC and TDF. Maybe not too big a deal if somebody is young not postmenopausal has other risk factors for osteopenia or osteoporosis. All right, and in a subset analysis, so here, we are looking at gender affirming hormone, hormonal therapy, and long-acting injectable pap for PrEP. So this was a subset of OA three, one they found is that there was low HIV risk perception and transgendered women. A lot of them did report being on gender-affirming therapy. And again, what they showed is that in transgendered women, that long-acting tab was statistically superior in decreasing HIV acquisitions, there's only two verses seven in the oral FTC TDF arm, and basically, it was safe in transgendered women, and there were no drug interactions. So that long acting Capitec revere is safe to give with hormonal therapy, be it testosterone, Ester dial, or even birth control. So I think, for all of us, we know that there's this huge gap in prevention. So about 1.2 million Americans are likely to benefit from PrEP, one in four sexually active men who have sex with men are at risk for HIV. And they estimate about one in five people who inject drugs or 73,000. persons may be candidates for PrEP. But there's this big gap and persons that are aware about PrEP, those are willing to use and then that then those that are subsequently given a prescription. So again, of the there's very few patients that meet eligibility criteria for PrEP that are actually given a prescription. So if we look at new HIV diagnoses across the US, so really, the HIV epidemic has moved to the south, so over half of all new diagnoses are in the southern US. But if we start to break down gender, race, age and transmission factor, so it's still predominantly male, predominantly black and Hispanic, predominantly younger folks. And still, the biggest risk factor for acquisition is men who have sex with men. So for itu, it's about 4%. And for MSM, n ind. And Id you, there's an additional 4%.

This PrEP to need ratio, basically, it's a indicator of the number of people that should be on PrEP over I mean, the actual PrEP prescriptions divided by the number of persons that should be on PrEP. So the lower the number, the higher the PrEP to need ratio, and that also coincides with the epidemic moving to the south. So the majority of patients that are prescribed PrEP to 25% majority, I mean, more are male, more are white, and more are between the ages of 25 and 44. So, you know, I think that's an access issue and I think it's a more community level issue. about marketing reaching the population and then getting patients linked to centers that can prescribe PrEP. So who meets the indication for being on PrEP, so sexually active men who have sex with men plus, you know, a sexual exposure, it could be a serial discordant sex partner. It can be inconsistent use of condoms, but I think the big one or low hanging fruit, as they say, is any STI within the past six months. Similarly, for heterosexual men and women, if they have a risk factor, either HIV positive partner in particularly not on antiretroviral therapy, inconsistent use of condoms, but also a sexually transmitted infection within the past six months. And then for persons who inject drugs, it can be sharing of use of, of, of drug injection equipment, or if they have, in addition, risk of sexual acquisition of HIV. And again, if one has sexual risk, in addition to injection drug use, and if you feel afterwards, you know, I mean, cabotegravir may be an option, then that's a shared decision with the patient. If we look at effectiveness for oral PrEP, it's really 99% for men have sex with men and heterosexual men and women. And then for persons who inject drugs, it's about 74, to 84%. And that was the estimated based on that big tie study. And again, that was just what to know, for beer alone. So the effectiveness may be higher. But I think consensus is that for injection drug use, or if the risk is through parenteral, that we really encourage daily dosing. So PrEP is effective if you take it so these are pulling the studies. And if you look at the effectiveness based on adherence, the more adherent the patients are, especially as we get into the 80%, the more effective any of the PrEP interventions are, and these are looking at these various studies. And this is really for oral PrEP. So why do we screen patients for acute HIV infection? Well, we really want to know, like, Pat, you know, is the horse already out of the barn. So we know that exposure to HIV, the first HIV of personnel that HIV sees is a dendritic cell ferries that to a regional lymph node two days, and then within the lymph node after three days more or five days from exposure than HIV spills into the bloodstream and become systemic, and that's when a person has symptoms of acute HIV infection. So it's important to screen patients so Chem sex, also known as party and player PNP refers to the practice of consuming drugs to enhance sexual activity, mostly among men who have sex with men. And really the most commonly used in the US is crystal meth amphetamines, more commonly in Europe are the ethnos or mephedrone, but we also have GH V, or GBL gamma hydroxy butyrate gamma UTRA lactone. So what's crystal methamphetamine, it's a chemical that has stimulant properties, lots of versatility, it can be crushed, inhaled into nasally. It can be dissolved in water injected intravenously or applied heat and it can be in inhaled, it causes the largest release of dopamine than any other substance known to man. So in contrast to cocaine, which just blocks the reuptake this one also blocks plus enhances direct release of dopamine. And the acute effects are kind of well-known now euphoria, arousal, paranoia, aggression, increased heart rate

and sex drive, decreased sleep and appetite. Interestingly, despite increasing libido, it also causes erectile dysfunction, and that's because of its anticholinergic effects, but it can enhance HIV transmission because of impaired decision making abilities. mucosal drying, those are the anticholinergic effects, and then also impaired immune function. So it can enhance those dendritic cells to pick up HIV and increased mucosal tissue sensitivity. So HIV positive men who have sex with men engaging in Chem sex are less likely to adhere to antiretroviral therapy. So therefore, we may have these bursts of increases in community viral loads. And in the hyper gay study, which looked at on demand PrEP, people who engaged in Chem sex were more likely to engage in higher risk practices that may have lead to HIV transmission, but they were actually much more likely to use On Demand PrEP correctly. And the open label proud study and Lendon demonstrated an 86% reduction in HIV acquisition among PrEP users. And of the 544 men have sex with men about 44% of those report engaging Chem sex. So again, chem sex is not a contraindication to any of the PrEP agents and there was no difference in adherence or efficacy compared with nonusers.

20:29
So how long is PrEP effective after you stop? So for FTC TAF, you may be able to maintain levels above or protective levels for 16 days after you stop. And for FTC TDF is 10. Typically the convention is after you stop really after about a week of stopping, you know, these levels may start to drop. So if there's been exposure beyond that, you may want to pet them before you PrEP them again. And for long acting cat, you want to re educate patients about the tail. So when a person stops long acting cab, the levels are likely to continue. So levels stopped being protective about three months from the last injection. But they continued to be present and in increasingly decreasing levels or sub therapeutic levels for up to 12 months. So you want to assess ongoing risk for HIV risk. And if PrEP is still indicated, I would say transition them to either oral PrEP, oral FTC TDF FTC tap beginning within eight weeks after last injection, and then continue with their follow up visits for HIV testing quarterly for 12 months. So again, that tail is 12 months or longer. I mean, unless they tell you listen, I just want to stop I'm completely just going to abstain from any behavior that may put me at risk. That would be really the only reason but I think my default would be to transition them to oral PrEP if they should decide that they want to stop with the long acting injectables. So the symptoms of acute HIV infection are fever fatigue, very influenza, like with rash, that could have some GI symptoms as well. You know, acute HIV typically presents within two weeks may present like COVID, which presents within two to 14 days, duration of symptoms are about the same. Some of the big differences is that with acute HIV, you have the absence of right of sinal pulmonary symptoms. Whereas with COVID, you have those and also that loss of taste or smell, which is not really present with acute HIV. PrEP really works if you take it if you have on time injections, the vast majority of HIV infections that are acquired while on PrEP are because patients are not taking the drug consistently. There's been very few cases of PrEP failure. And most of these have either been due to poor adherence or rare cases where the source virus had multi drug resistance. But you have

to contrast to hundreds of 1000s people who have really successfully taken PrEP. So lastly, here just I'm just going to this is the last section just comparing some of the clinical and logistical factors for which PrEP regimen to use. So for TDF FTC, all exposures, TAF FTC really limited to MSM, and transgender women really not approved for receptive vaginal, and not approved for injection. Cab is for sexual exposures and all adults, no data for injection drug use. And remember, now we can provide PEP and PrEP to adolescents in New York State. Time to protection. So for rectal exposure, it's seven days it's kind of the 21 seven day rule generally what they say is, you know, seven days really for rectal, everything else a minimum of seven, but it may be better after 20. And definitely for injection drug use, I would say at least 20 days. And then we also have the on demand. And then there's no data really for TAP FTC and for CAB LA. Generally the pharmacokinetic data suggests that after an injection, the majority of people will probably have protective level by two days. But that the 95% interval for the outliers is a week. So our recommendation is that you wait a week in order for the really majority of people to have protective levels in all tissues. And sometimes what we're doing and it's just considered a best practice is let's say someone's on oral PrEP and they want to train addition to long acting, and I'll tell them to extend their oral PrEP for a week after their first injection. All right, renal safety. I think we spoke about that. So basically, um, for TDF FTC, there's a GFR creating clearance limit of if it's less than 60. It's not recommended. For TAF FTC, you can dose to as low as 30 MLS. And then for Cab la really may be good for patients with renal insufficiency. There's no data and those with less than craning currents less than 30. So again, I think a good if someone has pre existing kidney disease either TAF FTC or cab la bone safety, I think if they've got pre existing conditions, you may want to move towards either Taff FTC or cab long acting. And again, if patients have pre existing risk for decreases in bone, mineral density, either TAF FTC or cab and then lastly some of the clinical differences, so for weights TDF FTC tends to cause weight loss and decreases in LDL. Taff FTC causes mild weight gain and small increases in L and LDL cab really mild weight gain but no significant changes in lipids. For TDF FTC daily dosing is preferred, but on demand dosing is an option. Tap FTC assists daily dosing for karabell A, you have the option for an oral leading, but most in the most in the field that just going direct to inject. You start off with two loading doses separated by a month. So it's baseline in a month and then every two months, and again for same day initiation. You can do that with either oral PrEP but really, with Cabot's not recommended just because you want to really make sure that that you have those negative results within a week before initiating. common adverse effects for these are diarrhea nausea for TDF FTC. And for CAB it's really mainly just injection site reaction. If someone is pregnant, or planning pregnancy, what has really the most data as TDF FTC. Again, we don't really have data for Taff FTC, nor for Kab long acting, although studies are underway. But if the benefit outweighs the risk, one could have a shared decision and continue with either long acting cap. Again, all of these can be used with oral contraceptives and also with gender affirming therapy. So again, all of these really can be used, and we really don't suggest that there are any drug-drug interactions. And then lastly, for patients with active chronic hep B, you want to use only TDF FTC or Taff FTC. Both of these antivirals have activity against active hep B

and KAB. La doesn't. So if someone is HIV negative, meets the indication for cat four PrEP and has active hep B, you want to use either TDF FTC or Taff FTC. So on demand, here's their cartoon, it's two tablets two to 24 hours before sex than 124 hours after and another 48 hours after it's really important those pre doses. So again, someone needs to have the bit of the choreography of like pre planning for an exposure again, not indicated for injection drug use. So PrEP guidance for people use drugs for injection, ideally, weenie one days of daily dosing of really TDF FTC on demand dosing is not recommended and insufficient data for either cab or really TAF as well. And for patient who use drugs nasally in inhalation only and they need protection from anal sex or insertive or even Yeah, receptive vaginal, you can do daily dosing for seven days. Now this is for the seven days is for receptive, anal and then for vaginal, you would not want to use Taff you would still use TDF FTC at least seven days but possibly 20 You may consider on demand dosing for those with nasal in in in inhalational. And also you may consider long acting tap.

29:43
Lastly here just to round up is HCV reinfection. So here's the an PrEP study 2015 to 2020 looked at HIV, negative MSM and transgendered people and just overall their incidence rates at one year these are HIV negative MSM The tentative study 1.9 per 100 person years overall rates of HCV incidents for primary infection it was one point note but for reinfection, it was 25.5. So again, underscores the need for routine HCV testing and prompt treatment for those HIV negative MSM ZZ that are initiating PrEP and even those with a pre existing H HCV infection and this is just basically what I spoke with before just breaking it out into potential risk exposures and which agent may be preferred. And this here just regimen specific so if someone has renal dysfunction, maybe tab LA or Taff FTC may be an option. If they've got osteoporosis may be tab or TAF, they got chronic hep B, just you know, TDF FTC or TAF FTC. If you want to just go for generic, then it's the TDF FTC. And then lastly, if a person has gluteal, fillers, silicone implants, you know, you can't use long acting and then for pregnant breastfeeding or planning pregnancy really the most data is with TDF FTC. So long acting injectables may help overcome some of these adherence challenges, but it has not been studied yet and people who use drugs, but in a quarter persons with opiate use disorders have strong interest in long acting PrEP. An interest was greater amongst female sex workers, those with recent visits to their providers and those with a high perceived risk for HIV. And then in the future, this big one is going to be Lenna cap Revere, it's a subcutaneous injection every six months and it is being studied in injection drug users. We also have these vaginal and rectal inserts, and broadly neutralizing antibodies which can be administered intravenously every six months but Lenacapavir is the one that I think is the most it's the closest to market and I will end there.

32:09
Thanks so much, Tony.
[End Transcript]