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PRE-EXPOSURE PROPHYLAXIS

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[video transcript]

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Rona Vail. Dr. Rona Vail is an HIV specialist providing medical care to HIV infected individuals for over 30 years. She has been at the kellen moore Community Health Center for the past 20 years where in addition to patient care, she has provided education and training on HIV to community members, students, residents and medical professionals. She serves on the New York State Department of Health AIDS Institute quality of care committee and serves as vice chair on the medical care criteria Guidelines Committee. Thanks Dr. Vail for collaborating with CIA and updating this course and presenting today. And I'll let you take it away.

00:44
Thanks so much. Sorry about the little computer thing. This is not my this is not my computer, I'm using our computer. So it's a little bit glitchy in terms of the controls, but hopefully it'll all work. Okay, let's get right into it. I have no disclosures. In terms of our learning objectives, they're here we're going to use we're going to review efficacy and screening testing best practices and the feature of PrEP today. But let's start with a question. So which of the following statements is false? A HIV incidence decreased by 9%? Between 2015 and 2019. HIV incidence is falling amongst all age groups. HIV incidence is falling amongst African Americans, or D HIV incidence is rising in transgender men and transgender women. So again, we're looking for the false statement here. All right. So this is one of those things where it's good that we're reviewing this because the, the answers are changing over time, which is a good thing. So the right the correct answer is, here we go. The HIV incidence is falling amongst all age groups, it is true that HIV incidence has decreased by 9%. And that it is falling amongst African Americans. And that is rising and transgender men and transgender women, let's take a look. So this is the trends by age. And what we can see is that it is falling amongst all age groups, except unfortunately, the group with the highest rates of HIV infection, which are 25 to 34 year olds, where the rates are stable in that group. So clearly, this is a group that we want to target for PrEP. And we look at gender, it is decreasing in both male and female, but not in transgender men or transgender women where the rates are continuing to rise. In terms of trends by race, race, and ethnicity, rates are dropping all across the board, except for some increases in American Native and Alaska Native individuals, where those rates are rising, but they tend to be low their overall. But in terms of plaque in African American individuals, what you can see is the rates are dropping, which is fantastic. But they're still the rates are highest there of all populations. And so that is a really important statistic in terms of looking at that, given the small percentage that Black and African Americans make up the general population in terms of about I think it's about 17%. And same for Hispanic and Latino populations, where the rates are much higher than in white individuals in spite of the fact of having representing a lower proportion of the population. So again, disproportionate effect of this epidemic. When we look further into the subpopulations, MSM, still tech still make up the majority of new cases, cases

69% of new cases are in men who have sex with men. And but you can see when you break that down further amongst MSM, it's really Black and African MSM that have the highest rates of new infections, followed by Hispanic and Latino followed by a white male to male sexual contact. And amongst women, Black and African American women are very disproportionately represented in affected by HIV. So communities of color are strongly disproportionately affected by HIV. Overall. And we talk about this, I talk about this because we have good HIV prevention, techniques and research, but we want to make sure we're reaching the folks who really need it. What we have right now, what we this is a little graph of what's currently available, what's and what's coming. I think what people know in terms of what's currently available is that everybody knows about condoms, syringe exchange programs, voluntary medical, male circumcision and HIV treatment for people living with HIV. HIV treatment for people living with HIV is also called treatment as prevention. I think by now most people are familiar with the term u equals u, which is undetectable equals on transmittable that if you have HIV and your viral load is undetectable, you can't sexually transmit that infection to a partner. A very, very important part of HIV prevention is getting individuals with HIV undetectable. But beyond that, we now have PrEP, Pre-Exposure Prophylaxis. Right now, our options are oral. And we have two options, which we'll be reviewing. But we have some exciting things coming some very soon and some a little further away. And we'll be talking about that a little bit more as well. But how will this PrEP work? Well, the answer the short answer is PrEP works. If you take it, if you look at this graph, and you look on the left side, on the vertical axis, you can see effectiveness percent and on the on the bottom horizontal axis you see detectable drug level. And what you can see pretty convincingly is that the higher the level of folks who have detectable drug level, so they're adhering to the meds, the higher the rates of effectiveness are in these trials and trials where adherence was very, very poor, we didn't see very good effect in trials where adherence was much higher, we saw a very good effect. And overall, the CDC estimates that for men who have sex with men and for heterosexual men and women, that if you have optimal or consistent use of PrEP, taking PrEP as directed, you will have a protective effect of about 99%. That's very, very highly effective as long as you take it. For persons who inject drugs, we only have a partial story. Unfortunately, there's only one trial, that trial only use TDF. It did not use TDF FTC. But only used one drug was one trial that was effective 74 to 84%. But we don't see the levels as high as in sexual exposures. But again, it's just one trial clearly a place we need more information, but it's but it is an effective intervention. So as I said, PrEP works if you take it and if you take it, you're going to be 99% protected, the vast majority of people who get HIV while taking PrEP, it's due to them not taking the medication consistently, the vast majority, there's really only a handful of cases six at my last count might be one or two more since then, since my last literature review, but about six cases of PrEP worldwide where somebody failed PrEP, but had adherence. So was taking had either dried blood spots or hair samples, plasma samples that were consistent with consistent PrEP, taking six, and that's hundreds of 1000s of people who have taken PrEP. So PrEP works if you take it. So the whole name of the game around effectiveness is about adherence. So given that, we have this great effective intervention, how are we doing in terms of getting people to take proud? Well, this is New York State's data as of June 2020. And as you can see, first of all, in terms of overall number of prescriptions, we're not there yet it the numbers are rising, which is great. But we're not there

yet. But what you can also see is that the rates are much, much higher in terms of individuals who are white accessing PrEP, but not other communities and communities of color. So we need to do a better job in terms of getting PrEP out and the same is true for gender. So clearly, we need to improve outreach, and address some of the social and structural barriers to PrEP and have a more equitable distribution of PrEP. Alright, so let's talk let's move away from epidemiology and talk about how to do PrEP. So I'm going to do this with a case. Naomi is a 27 year old transgender female who comes to you today to initiate gender affirming hormone therapy. She's taken street hormones that she's gotten from friends, but would now like to be medically supervised. She has no significant medical history. She's partnered with a cisgender male and also at times engages in survival sex to pay the bills, she uses condoms intermittently. You met we recommend PrEP for HIV prevention, but she's hesitant because she's heard that there's an effect of HIV medications on hormone levels. So your next question is, again, which of the following statements is false? Is it false that enough of your reduces estrogen levels, that estrogen reduces to enough of your levels. The false that the HIV rates and transgender women are about 49 times higher than the general population, or that stigma, discrimination and lack of employment opportunities lead to higher rates of sex work in transgender women. Which of these statements is false? Okay, so Georgia people think that tenofovir reduces estrogen levels.

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Let's see what the real answer is.

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It's enough of your reduces estrogen levels. That is the false answer. That is correct. So it is true that estrogen reduces to enough of your levels. We'll be talking about that. But the good news is that tenofovir and other HIV medications do not reduce estrogen levels. And so one of the things that's important or help can be helpful to do proactively is to say to somebody like Naomi, I know that you're concerned, but we really have good data. You're not your hormone levels are not going to be affected by this medication. And we have the studies to show it. In terms of HIV and PrEP and transgender populations, the rates in transgender women of HIV are very, very high 90% prevalence which is higher 49 times higher than the general population. It is true that stigma and discrimination and lack of employment opportunities can lead to higher rates of sex work, and there's just less awareness of PrEP overall in the transgender community. And the concerns about hormones and interactions do lead to some hesitancy to take PrEP. Even less is known about HIV and STI and PrEP for trans gender men. The prevalence of HIV varies in studies from zero to 3%. But as I saw before, we saw before the rates are rising prevalence of STI in more recent studies is is pretty high, six to 47%. sexual partners, a lot of transgender men have more fluidity around partnering. And so about a third will partner with males, only females only both males and females, all different kinds of bodies, and can have both anal and vaginal sex, and tend to have lower rates of condom use. So clearly population we want to be thoughtful about in terms of reaching out for PrEP. Alright, so let's talk about the guidelines. New York state guidelines were updated last year. So when I'm talking about guidelines today, and I'm talking about how to do PrEP, I'm really basing this on New York State's guidelines, the CDC is right now in the process of updating their guidelines, but

they have not been updated since the initial guideline was placed. And we've had a lot more data, a lot more information and a lot more experience with doing PrEP. And so New York State updated the guidelines. And I think these guidelines are great. And that's what we're going to be talking about today. Okay, upon hearing reassurance that PrEP will not affect your hormones. Naomi agrees to initiate PrEP. Can we give her a prescription today at our first visit? Yes, we can draw labs and then start PrEP? No, first, we need to be sure there's no contraindications to PrEP, and we need to get those lab results back. All right. Which do we do? Or can you give her a prescription today? Or are we going to wait for those lab tests results to come back?

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Actually, yes, good. So 64% That said, Yes, we can draw labs and then start PrEP today? And the answer is yes, we can draw labs and then start PrEP today. And that's a newer guideline, that that has only been true for the last couple of years. Before that, we would not do that. So in terms of the guidelines in the big changes from New York, in New York state guidelines from last year, it was it's really an attempt to individualize PrEP and make, reduce some of the barriers and make people give people just basically reduce the barriers to help get more people onto PrEP. The guidelines talk about same day initiation, dosing strategies of daily or On Demand, drug choice, Truvada, or discovering flexibility for frequency of follow up visits. And we'll talk about that we'll talk about all of this and testing at alternate sites. Just as we talk about the guidelines, just so you know, ci has these great free clinical cards, they're just a quick how to, you can pull out of your pocket and have all the most important relevant information right on a card. So go ahead and order them. And they're really quite useful. All right, so let's talk about same day PrEP first. The approval for use of same day PrEP really came from a lot from this study, which was a basically a demonstration trial at New York City sexual health clinics, where they made the decision to look at the safety of same day PrEP, and in their protocol, everybody started PrEP unless there was a potential contra indication. So if somebody had signs of acute HIV infection, they were not started. If somebody had a history of kidney disease, they were not started. And if somebody had a history of Hepatitis B, they were not started. Hepatitis B is not really a contraindication. It's more that may be coming out of the gate. lines. But it's more than that because 10 off of your does an emphasize to beam do treat Hepatitis B, want to make sure you know their Hepatitis status. And if they have infection, you might want to know about their liver. But again, the big contraindications are kidney disease and a signs of acute HIV infection. And we don't want to give PrEP to somebody who may be sera converting for HIV infection. Alright, so in this, in this project and this demonstration project, they had 14 137, PrEP candidates, almost all ended up being candidates for immediate PrEP. But 50 did have some contra indication some potential contraindications based on those three criteria, and so did not get started on the same day. So what happened of everybody who got immediate PrEP of 1437, only four ended up having to had an absolute contraindication had to stop. And all were able to stop within 10 days with absolutely no negative consequences as a result of that. In terms of delayed PrEP, of the 50, that had PrEP, delayed 43 were candidates, but only 35% initiated PrEP within 60 days. So the conclusions were that dispensing PrEP based on a medical evaluation is safe. And also the delaying PrEP results in a substantial loss to follow up. So as a result of this same day initiation, the overall goal in New York state guidelines is same day

initiation in patients without known Hepatitis B renal disease, need for PEP or signs or symptoms of acute HIV infection. And you can do same day PrEP, as long as you don't have one of those contraindications. And as long as you will follow up on those laboratory results within seven days, and that's key, draw the labs today start PrEP, but you have to act, you have to get those lab results and act on them within seven days in case somebody has is HIV positive on those lab tests or has significant renal disease and you have to adjust or stop medication, so you have to act on them within seven days. Nobody even if you have bad kidney disease, seven days of tenofovir is not going to cause a problem. And if you do have HIV, seven days of two drugs is also not enough to cause a problem in terms of developing resistance. As we can see from this study,

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this is the Thai Red Cross study, they do same day PrEP in their cohort 2442 started on the same day, everybody got a viral load at baseline and it turned out that seven of them had acute HIV infection, they had a positive viral load. Of those seven, three people did develop a mutation, but no mutations happen until day 29. Nobody who had their viral load seen acted on and addressed within 15 days developed a mutation. And so this gives us confidence in this kind of information gives us confidence that if even if somebody has HIV is too reconverting when you start them on PrEP as long as you intervene within that seven day period and intensify them to a full regimen, you're going to be okay. Okay, we now have two drugs that are available for a PrEP td td ffdc, also known as Truvada or Taff FTC known as D scoping. So which medication do we choose? Okay, I'm going to ask you that question. All right. Which of the following statements is true going for truth this time? TAF FTC, or disco v is the preferred option for PrEP due to its better safety profile. TAF FTC is approved for all sexual exposures but not for injection exposure. Both A and B are true or neither B neither a or b are true. Which do you think is the correct answer here? So this is something people aren't really sure about, which is exactly why we're reviewing this. So we've got answers all over the place. Let's look at what the correct answer is. And the correct answer is neither a or b are true. It is not true. The TAF is preferred because it's a better safety profile. And it's not true that Taff is approved for all sexual exposures. And we're gonna talk about those in detail. All right, but first, let's talk about the approval. The approval is based on a very large, randomized, double blind, active controlled phase three trial of TAF FTC versus TDF FTC. And what the study found is that taffet both performed incredibly well. Both were very effective in preventing HIV and Taff FTC was non inferior to TDF TDF FTC at 96 weeks and approval was based on that. But what about safety? That's always been a big issue right? There's been a lot of buzz a once TAF was approved there was a lot particularly like on social media. There's a lot of buzz that oh everybody should be on Taff at this point because TAF is less toxic, it's the better medication gets your provider to change you to Taff FTC going to SCOBY. And, you know, the reality is not, not that. So let's talk about that there are some differences and it is important, but let's talk about it. First off, anybody who's doing HIV care, knows and has seen cases, a case of somebody who develops renal tubular acidosis from tenofovir tenofovir can cause a renal tubular acidosis. However, in those, the majority of those folks have a lot of predisposition towards kidney disease, and we're on boosted HIV regimens. So HIV regimens like that are protease base or one of the integrators

use a pharmacokinetic booster to boost the levels of the protease or the integrase to make them more effective. But that pharmacokinetic booster also boosts the levels of tenofovir a little bit to make it less toxic. So in this meta analysis of the safety of unboosted TDF FTC versus TAF FTC, they took five HIV treatment trials that did not have a booster in them, covering 3100 And at one individual's and there was no statistically significant difference between Taff or TDF in terms of any serious clinical or grade three or four adverse events.

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Then we have a lot of safety data for TDF FTC. As in terms of PrEP, in all the studies of TDF FTC versus placebo, we have 22,730 person years of follow up. And so a lot, a lot of follow up of TDF for PrEP. And what you can see is there's no statistical versus placebo, there was no statistical difference difference in terms of grade three for adverse events, serious adverse events, fractures in grade three and above creating elevations, there was a very small difference in grade one and two, creating an elevation so there is a subset of people for whom there is a potential issue. And that's why discovery is a good thing to have, or tap FTC. So and comparing them more directly in terms of TDF FTC effectiveness is for TDF FTC has been established in all populations and all forms of exposure, whereas for TAP FTC, it's only cisgender men and transgender women. In terms of renal safety, there is a potential effect on renal tubular function for TDF. You do have to discontinue if you have a confirmed creatine clearance less than 54 Taff there are improved renal biomarkers compared to TDF. And you can be used down to a creatinine clearance less than 30. And so for somebody with pre existing renal disease or super high risk, you know, older kidney disease, older hypertension, diabetes, etc. This Goby to our to fftc may be the better option. Same thing for bone safety, there is a potential decrease in bone mineral safety, but meta analyses do show good safety, even in terms of bone. But for again, somebody who has pre existing bone disease, tough, maybe preferred in terms of metabolics, there's a little bit of differences favoring TDF where TDF is an FTC our weight neutral, there are a mild weight gain observed in studies of Taff very small about one kilogram or so. And in terms of LDL cholesterol, we know TDF actually lowers cholesterol where as Taff causes small increases in cholesterol. dosing is a difference, too. So for TDF FTC, pond demand dosing is an option for cisgender, MSM, and we'll talk about that, whereas for Taff, it's only daily dosing and a big difference now, so TDF, or Truvada went off patent. And there is now a generic TDF FTC available, and most recent pricing that I saw was about $39 for 30 pills, compared to $2,025 for 30 pills.

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Huge difference. So

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question, and for a question on demand dosing of teff TDF FTC, or taking medications just so on demand dosing means you're taking medication on demand meaning not daily, but just before and just after sex. Again, we'll talk about the details of that. So on demand dosing of TDF FTC, taking medication just before and after sex instead of daily has been shown to be an effective strategy for handle sex, vaginal sex, both anal and vaginal sex for neither anal or

vaginal sex. audience thinks Okay, so most people agree that it is animal sexual those some bad of the same proportion think it's okay for both. And so what is the answer? And the answer is only anal sex. So on demand dosing is not an option for vaginal sex and we'll talk about why. Okay, so this is straight out in New York state guidelines from as, as per the New York state guidelines TDF FTC is the preferred regimen for PrEP based on all the things we talked about, in terms of effectiveness in all populations, um, dosing, flexibility, cost, etc. It is the preferred regimen, but to fftc, once daily, is an option for prevention of HIV through sexual exposure and cisgender men and transgender women and is actually prefer is an option and is preferred, and people have pre existing renal disease or osteoporosis. And the guidelines for the first time so on demand dosing, I should say is not FDA approved as a dosing option. But guidelines have now endorsed it as a strategy based on the data. So even though it's an off label use New York state guidelines, the new CDC guideline update will include it as an option. international guidelines include on demand dosing of TDF FTC as an option for men who have sex with men. And let's talk a little bit about how one does on demand dosing. Alright, so on demand dosing was approved based on this large study called the Ebro case study that showed that taking medication before and after sex effectively prevented HIV acquisition and MSM. And so the way on demand dosing works, this is a graphic for if you have sex once a week. So let's say you know, you're going to have sex on Friday, late Thursday night, Friday, you know, you're going to have sex now. This is one of the first caveats about ondemand. dosing, you have to be able to plan for sex, because you have to take your pills, at least at least two hours and more, preferably closer to 24 hours before that sex. So two to 24 hours before sex, you take two pills to 224 to two to 24 hours before PrEP. Before presets, you take PrEP. Oops, sorry, did that mean to do that, and then you take another pill 24 hours after the first pill and another pill 48 hours after the first pill. So this is oftentimes called 211 dosing. Some people call this 211 PrEP. So it's two pills to 224 hours before and then one pill 24, and then 48 hours post sex. Well, what are your sex doesn't look like this picture, but it looks more like this picture. Right, you're having more frequent sex? Well, then it's basically to one one to 11111 until two days after the last sex, so it's two pills before and then one pill a day, until two days after the last sex if you're having sex on multiple occasions. And then, if you're going to have sex, again, less than seven days before, after your last tablet, you don't need that initial loading dose, you can just do one pill, two to 24 hours before, and then a pill 24 and 48 hours until two days after the last sex. Okay, so this is how you do on demand dosing for more frequent sex and the other was for less frequent sex. And, you know, needless to say, you know, on demand, PrEP means taking some time with folks and really helping to walk them through these scenarios and how to take it, teach back, etc, to make sure people have it. We have a little graphic that we give to people like this to help people remember so it's in their mind. And like I said, it has to be somebody who plans for sex, this is not going to work for somebody who has spontaneous sex. And so I'll just ask that right up front. So think about the last two to three times you had sex. If somebody is interested on demand, did you know you're going to have sex and you planned for it? Or did it just kind of happen? You have to be planning for sex for this

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to work. Alright.

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So this is the issue with vaginal exposures. Vaginal and cervical tissue just does not get the same levels of tenofovir particularly does for anthracite have been, but not the same levels of tenofovir as rectal tissue does. So you see the rectal tissue is in green, vaginal tissue in aqua blue and cervical tissue in light blue. And the left hand graph is after a single dose, the elimination over time, and you can see that that dose is that the levels drop much faster for cervical and vaginal exposures and predictable exposures. And emphasize means a little better, but it's just not enough. And so as a result of this traffic, you're not reaching the same levels of prevention of natural exposures really requires more like six to seven doses a week. And so adherence. For rectal exposures, we have data that says four doses a week is enough. Whereas for vaginal exposures, you really in the six to seven day week dosing much higher levels of adherence are needed for vaginal exposure, unfortunately. Alright, so just to review on dosing strategies, daily dosing is the preferred dosing regimen, but on demand is an option for cisgender MSM. On Demand dosing of tap FTC has not been studied tap FTC should not be dosed, as on demand until we have some data on that. On Demand, PrEP is not recommended for transgender women taking estrogen. Again, we talked before about the fact that that that estrogen reduces to enough of your levels. And we don't know if we know that the levels are good enough for daily PrEP, even though they're a little bit lower when you're on estrogen. But we don't know about on demand PrEP, so it is safer to go with daily PrEP for transgender women who take estrogen. It's also not recommended for vaginal sex, it's not recommended for injection drug use. And it's not recommended for people with Hepatitis B because you don't want to intermittently treat Hepatitis B what's enough a beer

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for sure.

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Alright, let's talk about the test we need to do. Recommended pre prescription lab test. So these are the test you're gonna do that first day, just before you write your prescription, you want to do a baseline HIV test, if you have the ability to do a rapid test in the in your clinic in your office, that's great. But you still want to send off a fourth generation test if you don't, and so but a rapid test is a great thing to have. But if you not don't have access to it, you can still do same day PrEP as long as you're getting that HIV test off to the lab and you're going to check it. So you're going to get a baseline HIV test. HIV RNA testing. So viral load, right, so the viral load is the test for acute HIV infection, because it turns positive, the fastest of all the HIV tests, right, it will turn positive eight to 12 days after General and on average eight to 12 days after an exposure. So it is recommended that we do viral load testing for anybody who's had an exposure within the past month, in case the HIV test the antibody tests or even the antigen antibody test is not reactive yet. So a viral load for anybody who's had a potential HIV exposure because as I said before, we don't want to give to drugs to somebody who's actually got HIV and is or C or converting. at all, I will tell you that at Callen Lorde, we just get a viral load on everybody as a baseline test not as an ongoing test unless it's needed, but as a baseline because not everybody either

remembers when you're less sexual exposure was or is comfortable discussing it. And so we just get a viral load as a baseline because we want to make sure there's not acute HIV metabolic panel, particularly looking for renal function, pregnancy tests for folks of childbearing capacity to have maternities. So definitely Hepatitis B you need to but also we'll look at HIV, I mean Hepatitis A HIV HCV, syphilis and STI screening, serum liver enzymes and a urinalysis looking for a cult renal disease.

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All right.

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As you're about to write a prescription for Naomi for TDF FTC, you remember to ask Naomi when the last time she had sex was, she replies that she had sex five days ago. So which of the following is true? So of course, if it had been three days ago or less, we could give her post exposure prophylaxis, and then go on to give Pre-Exposure Prophylaxis, what she's done with her four weeks of post exposure prophylaxis. But this is five days. It's outside the window for PEP, but it's too soon for an HIV test to be positive. So which of the following is true? So I'm using the window period. What? Hang on, I didn't read it yet. move you over, or move you down. Alright, since Naomi is in the window period, where no tests can accurately tell us if she has contracted HIV, we need to wait two to three weeks until an HIV viral load can tell us if she's HIV positive from this encounter. Or although Naomi is in the window period, and an HIV test cannot tell us if she has been exposed from this encounter. We should go ahead and prescribe PrEP. Which of the following is true? Now? I don't know where the poll is. I'm sorry. Oops. Yeah, it's sorry. Like I said, it's not my computer. And here's the answer. Oh, well, we don't have to do the poll. Here's the answer. Sorry about that. Okay. Most people did say B. Thank you. So it's true that there's a risk here. Right. It is true that Naomi may have early HIV infection. And we can't tell, because the average day to positivity of a viral load is eight to 12 days, but it can take up to 33 days. And an average fourth generation HIV test is 16 to 21 days, but it can take as long as 42 days for 99% of people to test positive even though the average is in there. So the cons of initiating PrEP are that seroconversion may be occurring, and we're initiating an incomplete HIV regimen. But the pros of initiating is that waiting risks additional exposures and risks, further delays in initiation. And that's a huge risk I have seen, I really have seen too many people with seroconverted, because they came in asking for PrEP. And they weren't given it because they were in the window period. And they told to come back in a month. And in the month, they actually had sex again. So they were told to come back the next month. And of course, the next month, they come back positive. So just start PrEP in New York state government to say initiate PrEP for patients in the window period, but have them returned in one month or repeat HIV testing. So at least if they're positive in that early window, you can catch it early enough to hopefully intervene and not develop resistance. Right. So in terms of HIV testing, in terms this is now this is ongoing monitoring, you already started the PrEP, this is now the follow up monitoring, you're going to do an HIV fourth generation test one month after initiation for individuals that hadn't any risk exposure within the prior month. And then every three months while using PrEP. We do a viral load when somebody has symptoms of acute HIV or is

interrupted PrEP in the past month and had a potential exposure in the interim, then we'll do a viral load as well. serum creatinine clearance is done three months after initiation. And then every six months thereafter, you may do it more frequently as somebody who has a higher risk of renal disease, Hep C we do at least annually, you know more if indicated. More if indicated pregnancy in individuals of childbearing capacity, as needed in a urinalysis annually looking for a colt renal disease. So Naomi, Naomi returns for a one month follow up, she's doing well with PrEP, and she is not Mr. Dosen, starting her only complaint to some annual discomfort and on testing, Naomi has is found to have anal chlamydia. And now you're second guessing your wisdom and recommending PrEP to Naomi and you worry that you have facilitated condomless sex. So this has been an issue that a lot of people talk about, there is a you know, concern of a lot of people that by giving PrEP, you're encouraging condomless sex and that increases STIs. And we don't want to increase STIs. So that is something that people will be concerned about complained about. And when somebody says comes in saying I want PrEP, because I want to stop using condoms. You know, there's oftentimes a lot of concern, and sometimes consternation even. But I'm going to try to convince you of a different scenario, which is the fact that PrEP plus screening could actually decrease STI rates as opposed to increasing them. And it's all about screening.

38:10

The issue is that people with asymptomatic infections and the majority of STIs are asymptomatic people will come in when they have a drip, they'll come in when they have a rash. But they're not going to come in some will. So people come into our center every three months for screening. But generally people don't come in for screening that often if they don't have any symptoms. But now you've got somebody on PrEP, and they're getting every three month lab test anyway, you get the STI testing, and now you're bringing people into care for sexually active and you're screening them and they're treating their STIs. This was a modeling study that shows if you look at the left hand graphic, what you see is that so the yellow is once every once a year STI screening. So even if you test only once a year, you're going to decrease the incidence of STIs over time, because you're getting people into testing that don't necessarily test once a year. And the more you increase the interval, you can see how much faster the rates of STI decline it's pretty remarkable how much screening will reduce STI rates. Their their model predicted that if 40% of people who need PrEP got it. And for then there's a 40% risk compensation in that 40%. So 40% of people who start PrEP, stop using condoms altogether. You would still have at testing two times a year you would still decrease gonorrhea by 42% and Chlamydia by 40% in the neck over the next 10 years. If you increase that screening to every quarter, there's a further 50% reduction. Even reducing condoms by 80%. Increase would lead to a decrease in STIs because you're screening. So screen screen screen. It's all about screening. Alright, Let's move on where the guidelines recommend every three months screening regardless of symptoms, you can always adjust that frequency if somebody's risk is really not that high. But the baseline should be that the baseline should be every three months. And then you can adjust it based on individual need. And three sites screening for sure. You know, all MSM and transgender women unless the unless it is declined, rates of STIs are much higher extra genitally meaning orally or annually than they are generally. Alright. Let's move on

to retention in care. One of the problems we've had is actually keeping people on PrEP. So we have we're having an issue with getting people onto PrEP who need it. But we also have an issue with keeping people on PrEP. And I'm really part of that has probably been the over medicalization of PrEP. You know, we're taking people who are healthy, and telling them, they have to come in once every three months to see us to have HIV testing, STI testing kidneys, every six months, whatever. But every three months visits in HIV treatment for somebody who's stable and healthy and on care in care. It's every six months now. So we're asking people with our HIV to come in more frequently than people with HIV, which doesn't make a whole lot of sense. So Oh, no, there's some testing on the speaker. So hopefully, we won't be getting a lot of extraneous noise. I apologize if there is there may be some alarms. Okay. So these guidelines really strongly commit to trying to provide flexibility in terms of in person visits, you can do video visits, but people really only need to come in once a year or twice a year, once. We have alarms, okay, I'm going to just talk over the alarms. People may. People who are who are stable on PrEP, taking crap in there don't have an issue really only need to be seen once a year, maybe twice a year, you can do an interim visit via video. But really, what you only need to do is like send your lab orders off to a lab. Maybe a lab is close to home or close to work. So folks can just do their lab testing at their convenience every three months. And then, and then only come in in person, once a year, twice a year or do video visits. So important to be flexible. Naomi doesn't show for her next quarterly print visit, PrEP should be held until we can confirm that she's HIV negative still true or false? So she doesn't we don't have that quarterly HIV test. So we don't know if she served them. But in that month

43:00

sorry about this testing of the speakers. Okay. All right. So most people think it's false about a quarter think it's true. And if you're going on on CDC guidelines, or old New York state guidelines, the answer was true. But now, we are saying the answer is false. And that, essentially, while well, routine HIV testing is an integral component of safe use of PrEP. If an individual taking PrEP misses a scheduled appointment, don't interrupt PrEP. I've seen too many people get HIV because they were on PrEP. And then they couldn't access PrEP, because they couldn't make an appointment. They couldn't make it to an appointment, they didn't have an HIV test, the provider wouldn't give them PrEP. Don't interrupt PrEP. Instead, encourage continuation of PrEP and work with the individual to reschedule any necessary visits in lab testing. Keep people on PrEP as much as possible. We know it's safe, we know it's effective. So the better safety measures to keep calling PrEP up until the point at some point, you're gonna reach a trigger where you're like, Okay, it's been too long, but certainly not immediately interrupting PrEP. So again, so you know, in until we before we go on to the future of PrEP, just in summary, these guidelines will hopefully help advance do some of the barriers and address some health equity in PrEP, we need to increase awareness, we need to recognize those barriers, such as mistrust of the medical system and HIV and PEP stigma. And we need to build capacity for trusted healthcare providers to provide PrEP as part of their services and to promote racial and ethnic equity. I want to take final minutes to talk about the PrEP pipeline. And what's coming. The PrEP pipeline is pretty exciting. We already talked about what's currently available. We have two products currently at the FDA for for approval. One is a

delivery and vaginal ring which we'll talk about and also a long acting injectable. But we also have other there are efficacy trials on To wait for other medications as well, which include other long acting injectables, other medications, preventive vaccines and implants, implants under the skin, like a normal anon for birth control implants for HIV treatment. This is some of the stuff that's closest in development. These are the things that are either in development or about to be approved. We're going to talk about the vaginal ring, I'm going to talk about cabotegravir. But just so you know, there is a pill there's a PrEP pill called is lateral view of being looked at as a once a month pill once a month, so you can take your pill once a month and have PrEP protection. If it works, it's in studies expecting results in two years. And there's also Linda kappa Vir, which is a once every six months subcutaneous injection, also being looked at those trials will be done closer to 2025. But some exciting long acting options and implants are in preclinical trials. So some exciting stuff. But let's talk about delivering and Capitec revere so delivering a vaginal ring. That is not perfect, but it is at least a woman controlled and inserted monthly ring that decreased infections overall compared to placebo, you can see not very good overall rates of in protection in the two studies. But in folks who are over 21, and particularly over 25, we see better adherence we're going to spend a couple more minutes talking about cavitary or cabotegravir is almost certainly coming in the first half of 2020 22. It is at the FDA is fully expected to be approved, and it is coming. So we will be talking more about this in the coming year as how we figure out about this. But so what is cabotegravir Capitec is a long acting injectable that is given once every two months for PrEP in these studies. So once every two months intramuscular injection.

47:07

This was a phase two B three randomized clinical trial HPT and only three in MSM and transgender women, this had very good diversity in terms of participation. They had over 50% were under 30 years old, they had over 10% transgender women in over 50% Black participants in the US. So some good diversity here. And basically everybody the first month got and this was placebo controlled TDF FTC, it was an active placebo. So TDF FTC vs injection, everybody got an injection of either placebo cam and everybody got a pill of either TDF FTC or for placebo. And everybody got first month got an oral lead in because we didn't know if there were going to be adverse reactions from the shot. And once you have a long acting injection in you, if you have an allergic reaction or some kind of adverse reaction, it's in you for a long time. So the first month is an oral medication. And then at week five, you're going to every two month injections for up to three years. Now. The plan study was for three years, but this was stopped early, because they saw a big discrepancy in HIV incidents for cabotegravir versus TDF ftc cabotegravir, with only 13 infections, whereas there were 39 and TDF ftc cabotegravir was statistically superior to TDF FTC. And it's all based on adherence. So it's not that it is the better drug it is that people took their shots, but people didn't necessarily take their pills as well as they needed to. So it's really about drug levels and drug adherence, but it was statistically superior. Alright, some of the big issues with cabotegravir are injection site reactions, that injection does cause a reaction that does happen in most people. But in most people, it is mild to moderate, you can see that the love the injection site reactions happen more frequently to begin with, and then decrease over time. And by the end of the study, very few people have anything more than

a great one mild infection injection site reaction and most people don't have any reaction at all. So your body gets used to it you get used to the idea of getting a shot. Very few discontinuations. And in spite of these injection site reactions in the initial studies of cabotegravir 97% of people chose to continue taking an injectable versus switch to an oral medication. So not bad enough for people to want to stop. The nice thing is we also have data on this for cisgender women in vaginal exposures. So HP to HPT and oh eight for was is a study in cisgender women. Also a large study also placebo control of TDF FTC also an oral lead in same setup QA weeks. And you can see this, this study has also been stopped early, because of the cumulative HIV incidents in TDF versus cabotegravir. So it's fully expected that this drug will be approved. The big challenges of this drug are going to be the logistics of it in terms of acquiring storing tracking patients, because the one of the problems with this is that that medication lessen your system over a very, very long period of time. So if somebody starts injections, and then they disappear, that medication stays in your system goes down very, very slowly over time, like over one to one and a half years, before it gets to undetectable. So it's sticking around for a long, long time. And then if you get HIV while your levels are dropping, you might develop resistance. So there are some caveats with this. So let me let Tara, take it from here. And then we can go to questions, if anybody has any.

Tara 51:06
So we have our first question here. Have there been any studies? Or are there recommendations for combining TDF FTC with depot Provera? And the impact on bone density for cisgender? Women?

51:21
That's a really good question. I, I am pretty close to certain, but I, you know, I don't do a lot of hormonal contraception. And so I'm not positive, but I'm almost certain there's not a significant interaction. With TDF, there have been more interactions in terms of dropping estrogen levels there. But you know, again, that's not my area of expertise. And in terms of bone density. So in terms of HIV treatment trials, we have data on cisgender females as well as men who have sex with men. In terms of bone density, it's an issue across the board where tenofovir can drop TDF particularly can drop bone density by about two to 3%, on average, amongst all populations, when it's used. So it is an across the board thing for most people two to 3% is not clinically significant, irrelevant. But if you already have pre existing bone disease, or super high risk for osteoporosis, then it can be.

Tara 52:26
Thanks so much. We'll get to the next question. And if we don't answer everyone's question, I'll send these over Dr. Bail, and we'll send out an email later with the answers. Absolutely. Yeah. So our next one is, when you talk about someone's risk exposure, would you just consider any sexual encounter? Or are you basing it off the various factors such as no knowledge of HIV status, no condom use, etc? I'm essentially asked me if you can, if you have to consider the window period for any sexual encounter?

52:57
That's a really good question. So first of all, of course, it depends on type of exposure, but also like who the partner is, if the partner is HIV positive? Are they in medicine? Are they undetectable? And how confident are you that you're getting the right information, but if somebody if your partner is HIV positive and undetectable, they're not going to transmit to you. So that's less of an issue than somebody who says, Oh, I took an HIV test three months ago, and it was negative, I'm more worried about that person than I am about the person who's HIV positive and undetectable. So it depends a lot on who your partners are, and the kind of sex that you're having. But I think overall, any any condomless sex, either anal or vaginal with somebody who may be at risk of HIV is is a is would be something I would consider for discussion of crap.

Tara 53:50
Okay, great. Thank you for injecting

53:52
that was for sexual intercourse injection use as well.

Tara 53:56
Okay, and we have two questions that are kind of similar, so I'll kind of read them in the same. Same thing. So the one question is, what would be your max timeline on a patient missing PrEP labs or appointments? Three, three months, six months? And then there's another question how long can you keep prescribing if they don't come in for testing? So kind of the same thing? What would be the patient timeline if they miss PrEP labs or, or anything?

54:24
I you know, there is not a right answer for that question. It is a hard one. It depends somewhat on, you know, are you able to reach the patient at all? Do they say yes, I've been taking it every single day and sorry, I've just been so busy. I can't get to the lab or I'm having childcare issues and I can't go but I am taking every day and I'm doing well versus somebody who's like just not showing up not answering your calls. You don't know if they're taking it or not. You don't know what their story is. You know, that feels a little bit different to me. I know I probably six months is an outer limit. But again, anytime you're always there's a risk there, you know, but three months is kind of up Best Practice, it's not nothing that we've ever done in a randomized clinical trial. It's just what we think is the right timeframe. So I think the more important piece is to not be so rigid around the three months. But the outside timeframe is really hard. I don't think there's a hard and fast rule about that. I'm just giving you my Gestalt about it.

Tara 55:18
Okay, great. Thanks. And we have one minute or two minutes left. So we'll have one more question. Are there still requirements to have specific number of sexual partners in order to be eligible for PrEP? Or is it the request for it enough to be eligible for PrEP?

55:32
That is such a good question. And it is absolutely the right question. Any, so we should screen people around sexual exposures, risk exposures, drug injection, use exposures, who people's partners are and what their practices are, to have a sense of who's at risk. Absolutely. But if somebody comes in saying I want PrEP, that's enough, self identified, being at risk for for HIV and wanting to start a PrEP is enough to start PrEP, but you don't have to prove that somebody needs it at all. That's a super important point. And I'm going to put a slide in about that. I used to have that but slide deck got too big. So as a really, really important point, and thank you for bringing that up.

Tara 56:14
Great. Thank you for the person who put that question. So thanks so much. Again, I'd like to thank you, Dr. Vail for presenting today. So thank you so much.

[End Transcript]