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STD Management in Primary Care: Best Practices and Practical Approaches to Reduce Risk

Narrator:

Welcome to CME on ReachMD. This segment, **STD Management in Primary Care: Best Practices and Practical Approaches to Reduce Risk** is sponsored by Vindico Medical Education and provided by an educational grant from Gilead Sciences. This activity focuses on the prevention of HIV transmission.

Your host and moderator is Matt Birnholz, MD, who is the Medical Director for ReachMD. Dr. Birnholz will speak with Dr. Raphael Landovitz, Associate Professor of Medicine and Associate Director at the UCLA Center for Clinical AIDS Research and Education in Los Angeles, California.

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Dr. Birnholz has nothing to disclose. Dr. Landovitz has received consulting fees from Gilead Sciences, Incorporated. He has contracted research with Gilead Sciences, Incorporated.

After listening to this activity, participants should be able to implement effective counseling strategies to motivate patients to adopt lifestyle modifications that may reduce their risk of HIV infection and utilize established guidelines to appropriately identify, treat and monitor patients who may benefit from PrEP to prevent HIV infection.

Dr. Birnholz:

You're listening to ReachMD, and this is Dr. Matt Birnholz. Today I'm joined by Dr. Raphael Landovitz, and we're going to be focusing on strategies for HIV prevention, both now and into the future.

Dr. Landovitz, welcome to our program.

Dr. Landovitz:

Thanks for having me.

Dr. Birnholz:

Great to have you with us. So, to start, can you provide us with a general overview, if you will, on the strategies used for HIV prevention?

Dr. Landovitz:

Sure. I think really having the conversation about what people are currently using to protect themselves against HIV is really three-quarters of the battle. I think a lot of providers are reluctant to bring up sensitive topics like sexual practices in a complicated and busy medical visit, but it really is critical to know how to direct them further to understand what they're doing, and so comfortability taking a

sexual history is critical to being an effective HIV preventionist.

The cornerstones of prevention have always been the use of condoms for genital-genital contact, but more and more in the current era we have really exciting additional strategies. We understand that the treatment of HIV-infected partners to undetectable viral levels with antiretroviral therapy is an incredibly potent HIV prevention strategy, so treatment really is prevention. In 2016, in emergency situations, where a condom failed and someone is of unknown HIV status and there's a need for sort of an emergency intervention, there's post-exposure prophylaxis. And we now also have a lot of information about pre-exposure prophylaxis or PrEP, which is a strategy, almost a birth control-like strategy, but for HIV prevention where people who are recurrently at risk for exposure to HIV can take a daily pill and protect themselves. Of course, mothers who are HIV infected can protect their unborn infants by themselves being on antiretroviral therapy if they are HIV infected, and that dramatically reduces the so-called vertical or mother to child transmission of HIV.

So, we have an enormous number of really exciting strategies in 2016, but unless you really begin the conversation with a patient, it's really hard to know how to guide them further.

Dr. Birnholz:

That's a great overview, and you started getting into pre-exposure prophylaxis or PrEP, and I'm really interested to learn more about that, specifically like the guideline history behind it, who it's recommended for. You touched upon that, but maybe we can get into that in more detail.

Dr. Landovitz:

Sure. PrEP, or pre-exposure prophylaxis, is this strategy of taking a medication on a daily basis to help prevent HIV infection, and for people who are HIV uninfected but are at recurrent risk, and right now there's only one medication that's FDA approved for PrEP. And just to be clear, PrEP is the strategy. The only FDA-approved medication is a fixed dose pill combination of tenofovir disoproxil fumarate and emtricitabine, which is known by the brand name Truvada. So, Truvada is an example of a medication that could be used for PrEP. We anticipate in the future there will be other medications that will be available for PrEP as well, but right now that's the only one that we have. That was approved in 2012.

And the CDC has actually issued clinical guidelines to help us figure out for whom this would be most useful, and it's actually FDA-approved for men with sex with other men who use condoms inconsistently, heterosexual men and women or injection drug users who have partners who are at high risk of being HIV infected or known to be HIV infected, as well as people who are in a serodiscordant relationship, which means one partner is positive and one is negative, and you can really think of a number of sort of customizable situations where people may be at increased risk for getting HIV. And when somebody comes into my practice and is requesting that they go on PrEP and they don't classically fall in one of the CDC guideline definitions, I often assume that even as comfortable as I may be in having a conversation about sexual practices, that there are often things that people are unwilling to disclose to even a provider who is sensitive to these sorts of topics. And so, after a detailed risk and benefit conversation with someone, if they really want to be on PrEP, I assume that there's something that they're not telling me that makes them particularly concerned about their behaviors.

Dr. Birnholz:

And I love how you took us back to the personal dynamic of the patient and physician relationship there and how this background and the guidelines intersect with clinical care, but I want to step back again to the evidence behind pre-exposure prophylaxis. What is it? What's out there?

Dr. Landovitz:

Yes, it's a great question, and I've had a number of people say to me, “Does that really work?” or, “What do we know about it?” or when I sort of tell people what the answer is, they say, “How can I not have heard about this?” So, there have been several efficacy studies that have informed our knowledge of how well this works. Among men who have sex with other men, or MSM, the first study that came out was the iPrEx study in 2010, and that had an estimate of 44% efficacy of daily oral Truvada compared with placebo, and a lot of people were disappointed by that result. And like any efficacy study, it's limited by how well people adhered to the intervention. Then it turns out, as it so often is the case, that if you don't take a medication, you can't expect it to work. And when they looked at biomarkers of people who actually adhered to the daily oral dosing -- and this was blood or intracellular levels of having taken the pill really at all -- the efficacy was over 90%. So, I think, it's safe to say that if taken as prescribed, the efficacy is at least 90% for rectal exposures, and some mathematical models even have suggested that if taken daily as prescribed, it can be as high as 99% for rectal exposures, which is a really exciting intervention in terms of an efficacy result. For vaginal exposures, the data isn't quite as well nuanced, but we think that, again, if you look at similar metrics of biomarkers, blood levels suggesting regular daily dosing as prescribed, that the modeling suggests that efficacy in vaginal exposures could be as high as 94, 95%, so again, over 90% for sure.

The difference between rectal and vaginal exposures are a couple of fold. We think that rectal exposures are more forgiving to missed doses, that you could get in as few as four or more doses per week and still get quite good protection against rectal exposures, whereas for vaginal exposures, you really need to be pretty near perfect to your daily dosing to get really good protection. Also, the timing of how quickly you get protected when you start is very different. For rectal exposures it's 5 to 7 days, and for vaginal exposures we think it's about 21 days, so 3 full weeks, so some important differences there but still very exciting data on how well this works.

Dr. Birnholz:

That's great. And you started getting into recommended prescription, the daily dosing. Can you give us some more detail about the dosing itself and the individuals for whom it's recommended?

Dr. Landovitz:

Yes, yes, so there's only one dosing regimen that's recommended at all, and as I mentioned, tenofovir disoproxil fumarate and emtricitabine, this fixed-dose combination only has one dose. It's 300 mg of the TDF, the tenofovir disoproxil fumarate, with 200 mg of the emtricitabine as a single pill, and it's administered daily with or without food. It's important before you start anyone on PrEP that you make sure that they're HIV uninfected, and you really want to make sure that the creatinine clearance is at least 60 ml/min. Below that, we don't have adequate safety data to recommend its use. And the daily dosing is really critical to emphasize to everyone.

The CDC gives us some practical guidance on how it should be done. My personal strategy is I like to see people monthly for the first 3 months, and those first 3 months I just do an HIV test and check the kidney function with a serum creatinine. And then after that 3-month interval, I back off a little bit and I see people on a quarterly basis, and at those quarterly visits I check for sexually transmitted infections; I still check kidney functions; and I, of course, check HIV status. I also always check for STDs before starting to make sure that I have appropriately treated any sexually transmitted infections that I find along the way since a lot of the observation is that PrEP use is associated with condomless sex, and so we are seeing high rates of STDs among PrEP users. Whether or not that's causal is unclear, or just because we're testing young, healthy people who otherwise might not be tested if they were asymptomatic remains a little bit unclear. But it's exciting to have people being proactive about their sexual health, in this way, and engaging them in the medical system, and we're finding all sorts of collateral benefits of having young, otherwise healthy, people being part of the medical system.

Dr. Birnholz:

For those who are just tuning in, you're listening to CME on ReachMD. I'm your host, Dr. Matt Birnholz, and today I'm speaking with Dr. Raphael Landovitz, Associate Professor of Medicine and Associate Director of the UCLA Center for Clinical AIDS Research and Education.

So, Dr. Landovitz, let's turn it back to the primary care provider and help reiterate why it's so important for them to understand PrEP as an HIV prevention strategy.

Dr. Landovitz:

Yes, I think it's a critical question. HIV providers may be the group of people who are most comfortable using these anti-HIV antiretroviral agents like Truvada or the next generation of PrEP agents that are going to be approved, but they're really not the people on the front lines who are going to see people who are HIV negative and at risk, so it really is going to fall to primary care doctors who are seeing people before they get HIV infected and where this intervention really has the most power. And I know I've heard from a lot of primary care providers that they are fearful of using these HIV drugs in negative people, that they're not comfortable with the side effect profile, but I think the CDC guidelines have really distilled it down into a way that's manageable. The side effect profile is fairly circumscribed. There's a gastrointestinal startup syndrome that about 20% of people get that is completely self-limited, usually goes to way after 2 to 4 weeks that can be managed symptomatically. There's a need for monitoring for renal dysfunction, which happens in about 2 in 1,000 people who take Truvada as PrEP, so just careful attention to creatinine monitoring is critical. And if creatinine clearance falls below 60, then stop it and wait for it to resolve, and people can often be rechallenged. And then there's a bone mineral density issue. One of the components of Truvada, the tenofovir disoproxil fumarate, is known to reduce bone mineral density, and we're not sure if calcium and vitamin D mitigates it -- that's being studied now -- but about 1 to 1.5% loss in bone mineral density in healthy, HIV-negative men who took this for PrEP, so knowing that is important. So, you might want to be extremely careful with people with a prior history of osteopenia or osteoporosis. And the good news is the bone mineral density loss appears to completely resolve when the medication is stopped. That was some recent data that came out at the CROI conference this past year in 2016.

Dr. Birnholz:

Excellent. And if we then move further in to the practice perspective of actually being in the room with the patient, identifying those patients that need PrEP is critical. So, how can clinicians go about doing that?

Dr. Landovitz:

Yes, it's coming back to the first question you asked me about really taking a sexual history and taking the time, even saying, “Are you in a relationship right now?” or, “Are you having sex with anyone right now?” and finding out who the partners are and whether people are using condoms for all genital-genital contact or what the barriers to condom use are, if people are having conversations about whether their partners are HIV infected or not and how they know, whether they themselves are getting tested. Testing is a form of HIV prevention, and I think that’s underestimated. CDC has guidelines that anyone age 13 to the mid 60s should be HIV tested once, and if they’re sexually active or at risk, tested more frequently. Sexually-active men who have sex with other men, even as frequently as every 3 to 6 months, is not unreasonable for HIV testing.

Dr. Birnholz:

And I'm sure that safety concerns also come up with PrEP. Obviously, some physicians, and perhaps even some patients, are aware of a case that was presented at a few conferences, I believe, that had to do with a patient that was taking daily PrEP and seroconverted to a multidrug-resistant strain of the virus. Now, is that something that the clinicians should be concerned about, and how common would this scenario be?

Dr. Landovitz:

Yes, thanks for bringing that up. This is a case that's gotten a lot of press, and so a lot of people are concerned about this. We did have the details of this case that have been talked about in the lay press extensively, finally presented at a scientific conference this past February, and so we know a lot more about it, and it's really an interesting case. It looks like someone who was taking PrEP on a daily basis, as prescribed, but was also having a large number of sexual partners and was having condomless sex and, apparently, was exposed to someone who had an extremely uncommon, but extremely resistant, strain of virus. And what's particularly notable about this case is not only is this extremely resistant strain an incredibly rare occurrence, but the fact that it actually was the transmitted strain is even rarer, so this is a vanishingly rare occurrence, which is why it's actually of a tremendous scientific interest, because this is a vanishingly rare occurrence.

So, in general, it's a reminder that nothing is perfect. No one ever said PrEP was going to be a perfect intervention. The best protection is still to use condoms all the time and use PrEP as your backup strategy, and this is an example of why, but this is certainly not something that means that PrEP doesn't work, that we should change our approach to using PrEP. It's a sobering reminder that nothing is ever going to be 100%.

Dr. Birnholz:

We only have a few minutes left, Dr. Landovitz, but before I ask you sort of to put on the prognosticator hat and get the crystal ball out and predict for us what you think the future is going to hold for this, I'd like to get a sense of some takeaway messages that you want to impart or re-impart to the primary care audience listening in right now regarding caring for at-risk patients.

Dr. Landovitz:

Yes, thanks. I think the most important thing is that the decision to go on PrEP or what to use for HIV prevention really should be a shared decision-making strategy. I think you're going to have a lot of trouble trying to convince people to do something that they really don't want to do, particularly in the “heat of the moment,” so working with people where they are with what they're comfortable with and getting them to be more comfortable understanding their own risk and feeling empowered to protect their own HIV negative status is really critical. And if that's limited to just getting tested, then so be it, and it can be a progressive conversation that you have over time. I think it's really problematic to shut down the conversation by being dogmatic and telling patients they need to do X, Y or Z. And so, being nonjudgmental and open-ended and really “pro” sex while really emphasizing the data about what we know about what works and what doesn't in terms of being effective for HIV prevention, and understanding both the risks and the benefits of each strategy in a nonjudgmental way, all begins by having the conversation. If you don't have the conversation, all of this allows myth and rumor and innuendo and false information that you can find anywhere on the Internet to persist and to proliferate.

Dr. Birnholz:

Great parting comments, and on that note, I do want to thank our guest, Dr. Landovitz, for helping us better understand HIV prevention and where we're at today and perhaps where we're going to be in the future. We focused on a number of great points, especially from a primary care perspective.

Dr. Landovitz, it was so great having you with us today.

Dr. Landovitz:

Thank you so much for having me.

Dr. Birnholz:

I'm Dr. Matt Birnholz and this is ReachMD. Thank you to all our listeners for listening.

Narrator:

This segment of CME on ReachMD is sponsored by Vindico Medical Education and supported by an educational grant from Gilead Sciences. To receive your free CME credit or to download this segment, go to ReachMD.com/CME. Thank you for listening.