# Expanding Access: Optimizing Use of Long-Acting Injectable PrEP

# CMEO Podcast Transcript

**David Alain Wohl, MD:**

Hello and welcome. On behalf of CME Outfitters, I'd like to welcome and thank you for joining us. This activity is titled, *Expanding Access: Optimizing Use of Long-Acting Injectable PrEP* and addresses global considerations, not just local considerations, but really thinking about this across the world. This is a program that's supported by an independent educational grant from Gilead Sciences.

So, today's activity may include discussion of products or devices that are not currently labeled for use by the United States Food and Drug Administration (FDA). And as a reminder, again, this is a program that's dedicated to thinking about things across the planet, so indications may vary by regulatory authorities across the world. So, clinicians should consult local guidance to confirm approved labeling.

So, I'm David Wohl, and I'm delighted to be joined by an incredibly super panel of discussants today that are going to share with me their thoughts. So, I'm going to start with having our panelists introduce themselves, and I'm going to start with Dr. Boonruang. And we'll allow each of these faculty to introduce themselves, tell us a little about themselves, and then we'll launch into the program.

So, Fair, I'm going to start with you, if it's okay. And we're going to be using first names, so-

**Jakkrapatara Boonruang, MD:**

That's fine.

**David Alain Wohl, MD:**

... everyone will get very familiar with each other. But let's start with you, Fair, and tell us about yourself.

**Jakkrapatara Boonruang, MD:**

Hi. Thank you, Dr. Wohl. And good morning, good afternoon, good evening, everybody. My name is Jakkrapatara Boonruang, or Fair. I am a Research Physician affiliated with the Institute of HIV Research and Innovation in Bangkok, Thailand. I provide sexual and reproductive health services, including pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), sexually transmitted infection (STI) prevention and treatment, but I am also privileged to be included as a sub-investigator in HIV Prevention Trials Network (HPTN) 083 and PURPOSE 2 studies as well. It's very nice to know you and to be talking in this panel.

**Cristina Mussini, MD:**

Hi, David. I'm Cristina Mussini. I'm Full Professor of Infectious Diseases and I'm the Chief of the Clinic of Infectious Diseases at the University of Moderna Reggio Emilia in Italy. I'm also a member of the governing council of International AIDS Society (IAS) and I'm the Vice Chair of the section on Antiretrovirus of the European AIDS Clinical Society.

**Landon Myer, MBChB, PhD:**

Hi, everyone. I'm Landon Myer. I'm Professor of Epidemiology and Biostatistics in the School of Public Health at the University of Cape Town. I'm a primary care physician, and I work largely in maternal and child health services, antenatal and postnatal care, as well as sexual reproductive healthcare for women in high HIV-burdened communities in South Africa, and work a lot in prevention and treatment issues facing these populations.

**David Alain Wohl, MD:**

So, our learning objective for today is listed here, differentiate between long-acting injectable PrEP options, including optimal patient selection criteria, transitioning strategies, and monitoring considerations. Thinking about which drugs and which people and how to match them together, that's really what we're talking about. And then once we do decide upon a strategy, what's involved with that? What's entailed, including monitoring and the types of things we have to worry about as far as toxicities or intolerance? So, we'll be getting more deeply into some of these questions as we move forward.

So, the first one, of course, is candidacy. Who's the right person for PrEP? And so, this has been something, again, that a lot of us have been thinking about, and again, in different parts of the world, we may think about this a little bit differently. So, I'm going to first choose Landon, and I'm going to ask, Landon, looking at when we think about who is, who do you think, where you are and what you're thinking about, which is really an important place to think about prevention, of course, but thinking about who's the right person, who stands to benefit the most from PrEP, and especially from long-acting PrEP, because a lot of what we're talking about today is how do we think about PrEP within the context of newer choices vis-a-vis long-acting injectable PrEP.

**Landon Myer, MBChB, PhD:**

Yeah, David, happy to share my thinking. And obviously we're here because everyone at increased risk of HIV acquisition needs to be thinking about PrEP with their providers. And that's true of long-acting agents from my perspective as well. That is, long-acting agents, they're incredibly efficacious and they have some really desirable properties that almost any dyad of a patient or provider should be thinking about long-actings. And the issue that we grapple with, and I think many regions of the world grapple with, is one of access. That is, if there's limited access for structural reasons, for financial reasons, for whatever set of health systems reasons, how do we think about patient prioritization? How do we think about who may benefit the most? So, everyone can benefit, but who would benefit the most?

And there, I think this slide does a great job of outlining some of the populations that might stand to benefit in excess from long-actings. People who have demonstrated challenges with oral PrEP is clearly a great population to start with because presumably these are patients, in my experience, who want to take PrEP, were interested in PrEP, and for whatever set of reasons, it might overlap with some of the psychosocial issues around seeking discretion to reduce stigma, or for other reasons, they're struggling with oral PrEP. And for me, that's a great starting place in terms of prioritizing long-actings because you've got a patient population who knows about PrEP, who appreciates PrEP, and then may struggle with orals and can take the next step into long-actings. And so, for me, people established on PrEP making a transition who are struggling is a good place to start, certainly.

 

**David Alain Wohl, MD:**

Yeah, no, I was just going to ask you a little bit more about that because I think that's great. But a minority of people take it, and you have experience now giving long-acting injectable PrEP to people in South Africa.

**Landon Myer, MBChB, PhD:**

Yeah. And I want to say, I think it's important to recognize that all PrEP is great. And like a lot of daily oral agents, when taken regularly, they're highly efficacious, but we know that across all treatment modalities, not just around HIV prevention, people often struggle to take daily treatments.

And so, as you say, the hand-raisers are a really important group. And what we find is that in transitioning to long-actings, the people who are established on orals and want to transition make for a very adherent long-acting patient population because they appreciate the modality that they're receiving. They know the alternative, in a sense, and appreciate the treatment modality, appreciate less frequent clinic visits, appreciate the discretion and potential for reduced stigma.

And so, I think that's a very good starting place to think about. It's certainly not the only one, however, because there are people who may be initiating PrEP who, for different sets of reasons, would certainly benefit from long-actings in particular. And the groups that I work with and think about a lot are mainly women, women of reproductive age, either during pregnancy and postpartum or outside of the context of pregnancy.

And those two issues that I wanted to surface here, the first is to recognize that pregnancy and postpartum is a time of radical changes in lives and in a woman's life and in a circumstances and living circumstances, sleep circumstances, and the ability to adhere to any daily therapy or daily prophylaxis. And so, it stands to reason and it resonates with our experience that long-actings could fit in well in this context. And then in the postpartum period is the place that I really believe that long-actings have a particular niche that women, we're recognizing, are at increased risk of transition. In many communities, there's new partner acquisition, there's ongoing breastfeeding transmission risk if there's seroconversion taking place, and so there's a really good rationale to have highly efficacious PrEP in the postpartum period.

And that dovetails with the second issue in women's health that I think long-actings are positioned to key into, which is the tradition of injectable contraceptives. Across sub-Saharan Africa, there's a very strong practice of administering injectable contraceptives. And so, women of reproductive age are well familiar with the notion of going to the clinic or seeing a provider to have a once every 3 months (Q3-month) or once every 6 months (Q6-month) injection, or a once every 2 months (Q2-month) injection in some instances.

And so, there's almost a tradition that in many parts of the world, certainly in South Africa, that we're seeing long-actings feed into for women of reproductive age.

**David Alain Wohl, MD:**

Yeah, no, it's great. And I love that idea of piggybacking on opportunity and also, of course, the scaffolding of contraception.

Of course, some people may not know about which agents we're exactly talking about and what the options are now. So, I think, Fair, maybe I'm going to call on you and ask you to maybe walk us through a little bit, because there are a bunch of different options, and you've been intimately involved in helping to study and compare

 

these different modalities for PrEP. So, maybe here we can just think a little bit about, well, what's on the menu? What are the options that we have that we can select from?

**Jakkrapatara Boonruang, MD:**

Definitely, David. Thank you very much. And yes, we are fortunate that we are now living in the era where exciting new innovations on PrEP are blooming. Before, we had oral regimens of PrEP, we have two of them, actually, tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and tenofovir alafenamide (TAF)/emtricitabine (FTC), or T-A-F/FTC, which are effective prevention tools on their own rights. For TDF/FTC, oral PrEP can be used in a daily and on demand or even driven manner. It is a very safe medications but still poses some effects on kidney functions and bone mineral density, while TAF/FTC had less effects on them.

However, we are introduced quite recently with long-acting injectable PrEP, including cabotegravir, or CAB-LA, and lenacapavir long-acting PrEP, or LEN. Both of these innovations have superior prevention efficacies than compared to the oral TDF/FTC daily regimen. The differences were CAB-LA, it requires an intramuscular injections every 2 months, except from the first month, where the injections would be one month apart. And LEN actually requires subcutaneous injections every 6 months.

We also have dapivirine vaginal ring as well, which has a modest efficacy but can be locally administered by inserting through vaginal canal every month.

**David Alain Wohl, MD:**

Yeah, for sure. Thank you for that overview. And I think it's important that you pointed out that the comparative studies, including those that you've been involved with, do show that long-acting injectable PrEP actually performs better than oral PrEP. And largely that's due to adherence. I think that's important to recognize that it's not so much that molecularly that there's one that's more potent than the other, but that it's just much more acceptable to folks. I think that's pretty consistent even in clinical practice subsequently, reflecting the preference data that we already just started to talk about, which I think is pretty clear.

So, the first long-acting injectable, as you mentioned, was cabotegravir for PrEP. And Cristina, I'm going to ask you to think a little bit about this with us. And I know we in the U.S. really adhere to the Department of Health and Human Services guidelines. You have the European AIDS Clinical Society (EACS) updates and the EACS recommendations, and I think it'd be helpful for us to understand a little bit about what's been updated more recently about long-acting injectable PrEP with cabotegravir. And I know that it's not only the efficacy data that have motivated some of the recommendations regarding CAB-LA, but also some of the data regarding stigma disclosure and even patient satisfaction in people who have been in the studies that have gotten CAB. So, maybe you just highlight a little bit from EACS what they've updated more recently regarding long-acting injectable CAB.

**Cristina Mussini, MD:**

Yeah, David. During the last Paris conference, we have shown the 21st updated version of the EACS guidelines. I have to say that we had a huge discussion because at that time, neither cabotegravir or lenacapavir were available in Europe, and usually we don't recommend anything that is not available in the continent. While we decided that we wanted to be positive and we decided to include long-acting PrEP in the updated version, I have

 

to say that we tried to cover all the aspects, as you said, because there are very positive aspects that are the decrease in stigma, because we don't have only to think about stigma of people living with HIV, but also people who are on PrEP. They think that their sexual life is under scrutiny when they come and that they under... There could be people who are judgmental. And so, I really think that even just not taking the pill either on demand or every day helps you in a way in facing in a positive way the stigma.

On the other hand, and also the preference, because I think that it's very important that in all trials, I heard talking about women, as Landon said, all the oral PrEP trials on women failed because they didn't take it. So, it's not surprising that women really, either because they are familiar with injection with the contraception or because of stigma or because they don't have to have pills all around the house when they have kids or whatever, I think that it's very important for them to have... It's really a huge opportunity.

On the other hand, we have also challenges. We don't have to forget that we have challenges. We have challenges concerning, for example, the risk of failure and of resistance. I still think that as the data showed, people, especially women but also men who really were adherent to schedule, to injection schedule, the risk of failure was very, very, very low, even zero infection in those who really adhere among women. So, I think that this is something that should be kept in mind.

On the other hand, we know that if the administration is more erratic, we know that we have a tail of cabotegravir. As we were saying about some pharmacokinetics (PK) issues, we have a tail that could last even for one year. We have to be very careful in counseling and telling people that if they discontinue injectables, they could acquire HIV in the presence of the drug, and so developing resistance. So, it's very important that there is a transition to the oral very, very soon.

And also, the fact that there is a development of genotypic resistance associated to the drugs that are in first line in all the guidelines, it's also something that should be evaluated. On the other hand, we have the great data on patient satisfaction and the impact on the quality of life. I think that injectables are for those who really want them.

**David Alain Wohl, MD:**

Yeah, no, that's a great point. I really like what you said. And I think it really is important to not prejudge whether or not somebody will say yes or no to an injectable and that it should be more universally offered because our own biases or filters may get in the way of equitable offering of newer advances in therapeutics and prevention. So, I think it's a really important point.

But I think it comes back to, and again, the EACS and U.S. Public Health Service guidelines, and in the United States and others, they look at data. And real briefly, maybe just give us a minute of an overview. But we're going to talk about four major trials in the next few minutes, and two of them have to do with cabotegravir, and that's the HPTN studies 083 and 084. These are really incredible studies, remarkable studies of the decade. So, I know it's a tall order, but Cristina, if you can just give us a thumbnail sketch for a minute or so about 083 and 084 and why they're so important and why they did put cabotegravir on the map.

**Cristina Mussini, MD:**

Yeah, I think that it's very important because these are two Phase 2, 3 trials, and they were double-dummy, so the results that they have are really reliable. And in HPTN 083, the population was composed by cisgender men

who have sex with men and transgender women who have sex with men and with a high likelihood of acquiring HIV, because they were a role in country with a high incidence to HIV, that is Argentina, Brazil. We know that Peru, we know that we have a very big problem in South America, South Africa, Vietnam, Thailand, and in the U.S. While the HPTN 084 included women and women in Africa, so Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, Zimbabwe, as I already talk about how it's challenging to have oral PrEP in women.

So, it's not surprising, since both trial versus oral PrEP, that the results in women was even more relevant than in men who have sex with men (MSM), because it was 88% of reduction in HIV incidents among women. And I have to say that for those who adhere to the schedule of injection, it was zero infection. So, this is very, very important. And also, when they look at the few cases, one case of infection was at baseline, so even less that it was reported. It was four, so it was actually three during the trial. While among MSM and transgender women, the incidence reduction was 68%. Both of them were really superior. Both trial were superior to oral PrEP. And also in men who have sex with men and transgender women, we had one of the infection that was baseline case.

So, I think that having two huge trials, two really milestone as a trial, both showing superiority to oral PrEP is not something that should be excluded from guidelines. And so, I think that this is something that we have to keep in mind, and it's very, very important. And the tolerability was very good. It was just the injection site reaction, but this is normal. It's an injection. But the rate of discontinuation was very, very low.

**David Alain Wohl, MD:**

Yeah, no, great. Wonderful. So, really, two very important trials showed the superiority of CAB compared to oral PrEP, and I think really important studies in basically all different types of people that you can imagine using PrEP in.

So, Fair, I think that was great and that put long-acting injectables on the map, as we said, but then we have lenacapavir, which is the next drug that became under scrutiny and tested in clinical trials. I think a lot of people don't realize that there's a twice-a-year injection that can prevent HIV infection. So, maybe just walk us similarly through long-acting injectable PrEP with LEN. And again, I've looked at lenacapavir and interrogated it across a broad diverse population that could benefit from PrEP. So, I'll turn it over to you.

**Jakkrapatara Boonruang, MD:**

Right. And lenacapavir, I think, follow the footsteps of what have been conducted with CAB-LA. They learned a lot, I believe, from the first ever long-acting injectable PrEP, such as CAB-LA.

So, lenacapavir also consists of two pivotal studies as well, PURPOSE 1 and PURPOSE 2. As for PURPOSE 1, this study will consist of the study population on cisgender women in South Africa and in Uganda, while PURPOSE 2 study covers a wider range of populations that including cisgender men, transgender women, transgender men, and gender non-binary individuals who have sex with the partners assigned male at birth. However, the efficacy of lenacapavir when compared to the oral PrEP, whether it be of TDF or of TAF, is very much astounding because in PURPOSE 1 study, there are no incident HIV infection at all among cisgender women in South Africa and Uganda, which is mind-blowing. Such amazing innovations. However, in PURPOSE 2, we've also find a few HIV incidence cases, but that also contribute to the reductions of 96% of HIV instances when compared to the baseline HIV incidents in the country that the study has been conducted.

So, those are the summary of very bird-eye views of PURPOSE 1 and PURPOSE 2. Generally, lenacapavir is a very well-tolerated innovations, but of course there is no innovation without limitations. So, in PURPOSE 2, we have commonly seen, of course, adverse events, particularly injection site pain, nodules, and redness. However, they are mostly mild. However, we do know that only 1% has discontinued the study because of this injection site reactions. So, in a way, we can imply that lenacapavir is a very well-tolerated innovations.

**David Alain Wohl, MD:**

Yeah, no, thank you. That's great. Again, so really wonderful.

Landon, I might just ask you just a little bit of an editorial comment, if you will, on PURPOSE 1 and PURPOSE 2 and what it's meant for you.

**Landon Myer, MBChB, PhD:**

David, if I might editorialize, I think four things really come to mind when I think about the PURPOSE trials. The first is, as Fair said, the remarkable efficacy. The second thing is the increased efficacy or evidence, both in CAB and LEN, for increased efficacy in women versus men. Again, very different, as Cristina says, from some of the other data that we're accustomed to seeing and that I think is exciting in that regard, and maybe needs a little bit of unpacking over time. The third thing I'd say is about the pregnancy data, because there's a lot of concern about the pregnancy data. And it's important to look at safety signals, absolutely. And as far as we know from the best available evidence, there aren't safety signals right now, and Phase 4 work has to keep going, of course. But this, by all accounts, is a safe agent in women of reproductive age.

**David Alain Wohl, MD:**

So, just recapping, we have two great options for people. We have long-acting injectable CAB, cabotegravir, and then we have long-acting injectable lenacapavir. The differences, as we highlighted, both work really well compared to oral PrEP, which definitely had its limitations and people voted with their injection sites, so it's great. But there are differences. So, CAB-LA, which came out first is intramuscular (IM). We give a dose of IM, and then a month later, another dose of IM, and then we're off to the races every 2 months. With twice yearly lenacapavir, there's some differences in the injection site reaction, as Fair mentioned, and I think those are important, more short-lived with CAB than with lenacapavir, which those nodules can persist. So, that's where we are.

So, what about what's coming down the pike? Because again, we've had this a great advance over the last few years from taking a pill a day basically to prevent your HIV, which a lot of people struggle to do, especially those who don't take any other pills who consider themselves healthy and don't really even see a doctor very often, to now something that could be taken, like we said, like contraception intermittently and with a shot. But there's probably even room to go, as I think we can all imagine, and maybe the perfect PrEP we haven't achieved yet.

So, I think some of the key considerations now that we should focus on, now that we talked about who's the right person and what are the products that are available that weren't available before, but I do also think we have to think a little bit about the mechanics of initiating PrEP, especially long-acting PrEP and how that can differ in some ways than what we've been used to before.

 

So, Fair, I might start with you, again, just going in order of what we've talked about before, is some of the key considerations when initiating PrEP now and some of the things we have to think about what we should really be paying attention to.

**Jakkrapatara Boonruang, MD:**

Definitely. Thank you. So, of course, we are looking at HIV testing before we start anything, including oral PrEP as well, but that is where the discrepancy happens because guidelines across the world recommend different things for HIV-negative status for innovations, such as long-acting injectable PrEP. So, in some countries in the world, they would recommend HIV nucleic acid amplification test (NAAT) tests because that, of course, is more accurate in terms of detecting HIV infections. But in some resource-limiting countries, such as in the Southeast Asian countries, we might not be able to do so, so we might have to rely on the fourth generation in the HIV testing instead. And this allows resource-limiting settings to be able to scale up long-acting injectable PrEP by utilizing the similar infrastructure as they had before for oral PrEP. So, I think fourth generation in the HIV testing in resource-limiting country is a very good way to go.

**David Alain Wohl, MD:**

And let me ask you a quick question, Fair, because this comes up a lot for us, is how long before you give the injection do you want to see a negative test?

**Jakkrapatara Boonruang, MD:**

Luckily for our settings in Thailand, we are able to get the result back in 1 hour.

**David Alain Wohl, MD:**

Oh, wow.

**Jakkrapatara Boonruang, MD:**

So, the result is quite fast. That might not be true with all the different settings, but with us, we don't have to answer that hard questions where we have to leverage the waiting period of time. So, 1 hour is actually acceptable in our client's perspective.

**Cristina Mussini, MD:**

Yeah, no, it's the same. It's just 1 week.

**Landon Myer, MBChB, PhD:**

To concur with Fair, the allowance for fourth-generation antigen and antibody testing really enables implementation in low-resource settings in a way that isn't necessarily an issue in Europe or North America. And so, same-day testing is routine in our setting. And if we couldn't use same-day testing, it would be a major health systems barrier to implementation. And our approach is really to initiate PrEP with the client in front of you on the day because often you can lose people, and so to do what you can in the moment.

 

**David Alain Wohl, MD:**

So, maybe I could just ask again, each of you, whether it could be what you're doing or what you think should be done if you are not doing it right now, because again, everywhere LEN is still just rolling out.

So, Landon, I'm going to start with you. Any thoughts about the cadence of HIV testing, given the newer modalities?

**Landon Myer, MBChB, PhD:**

Yeah, I think part of the problem with understanding the cadence of monitoring with LEN is that we don't have enough experience with breakthrough infections because it's so efficacious. It's kind of a … We're cut by our own sword in that sense, is that we don't know what to do because we haven't seen enough of it. And long may that continue. But I think a 6-monthly testing at the next injection, it just seems sensical from my perspective. In the absence of good data on LEN, because we don't have enough infections, I think it makes sense. What I think it will do in country programs is push country programs or districts or services to either CAB or LEN rather than to in a given patient population have a mix of them, because you could imagine that could lead to a little bit of chaos and implementation.

**Jakkrapatara Boonruang, MD:**

In my view, I think every 6 months screening for chlamydia, gonorrhea, and syphilis is sensible and it ties in perfectly with lenacapavir, but we can remain pragmatic. So, for example, a person comes in and they have symptoms. They can visit the clinics earlier and make that clear that clinics are not actually for every 6 month, but it can be more frequent than that if the sexual behavior calls for it. So, I think we can look at it differently this time where we can assess things separately.

**David Alain Wohl, MD:**

Yeah, that's great. So, we're talking mostly about initiating and then monitoring. We should recognize, of course, there's a bunch of people who are on oral PrEP who now, once injectable PrEP becomes available, are interested in switching, what to do when switching from oral to injectable. And one, I think, important thing to recognize is that one of the nice things about the injectables that I think most people don't appreciate is the level of protection you get is achieved very, very, very quickly. So, it's not like there has to be built up over a long period of time an accumulation of drug, and then you start to get the protection. When you look at the PK for both LEN and cabotegravir, it is remarkable how high the levels are even within the first day of administration. Coordinate this so that it makes a lot of sense that we don't want them to stop their oral PrEP a month beforehand, those kind of things that I think just make a lot of sense.

We've talked about oral lead-in for lenacapavir. We haven't talked about oral lead-in for cabotegravir, which was in the initial clinical trials. That was much more for a safety tolerability, not really for PK. And so, we've learned you don't really... Adverse events like allergic reactions, things like that to cabotegravir, it just hasn't really become an issue. So, doing an oral lead-in to test for cabotegravir, we don't need to do that. You can just go to direct to inject. But for lenacapavir, we do need that oral dosing to try to kickstart the levels that we've been talking about. And then once that occurs, then we can then transition just to the injectable and get on that cadence we were talking about.

 

I just want to check in with our faculty. Any thoughts about that or anything to add or your own experiences?

**Cristina Mussini, MD:**

No, we agree.

**David Alain Wohl, MD:**

Okay.

**Cristina Mussini, MD:**

We totally agree that everybody has the right to say no. I think that this is a very important sentence.

**David Alain Wohl, MD:**

No. So, don't let that get in your way. Don't let that be an obstacle.

You know, we talked about … I'm glad we jumped on this before about the STI screening. And Fair, you brought up some really good points about being pragmatic about it. I don't think we have to go too much in detail, but we do have an opportunity here to think not just about HIV. And I do agree, lenacapavir is so efficacious. I'm not worried about people acquiring HIV over the 6-month time period between their injection and their next injection. But we are worried, of course, about people acquiring syphilis or gonorrhea or chlamydia. And again, I think that there's been some guidance about what's the right, again, cadence in screening for sexually transmitted infections. And again, that differs now, the opportunity to test for that.

So, Fair, anything you want to add to that? Because I know you think about this a lot.

**Jakkrapatara Boonruang, MD:**

Yes, David. So, of course, I agree. We have to remain pragmatic but also prioritize STIs as well. What I think is possible as well is to do self-testing for STIs. We are now having a lot of combos between HIV, syphilis, chlamydia, and gonorrhea self-collections, and even self-testing. We can actually utilize that. If these innovations will also be included in the national guidelines and international guidelines, that would change the landscape of how we look at STIs around the world. So, that's going to reach people even in places where they cannot access physically to the clinic too. So, I think there are a lot to gain if we were to explore these options in the future.

**David Alain Wohl, MD:**

Wonderful. I think there's guidance that is in the package inserts for each of these products that I think spell this out that I think are a great place to look at some of the details. But again, I do think it's important for people to recognize that there are going to be situations where people either have a planned delay, "I'm going to be out of town," and you have to come up with a plan B for those people proactively. Or you might be in a situation where something happens and somebody has missed a dose, and now it's outside the window of where you think that that protection from the previous dose would still be present. So, be familiar with this, know what to do, know that your staff knows what to do, and I think that will get you in good stead because people are complicated. This will happen.

My only point here is that we have to recognize that there are a lot of these drivers of health that are structural. So, Fair, I might choose you because I think that you probably work in an environment that's very different, I heard already, from the one in which I work, which is definitely challenging. So, maybe you could talk a little bit about social drivers of health and how that plays out in your own practice, again, vis-a-vis delivery of PrEP and long-acting PrEP.

**Jakkrapatara Boonruang, MD:**

And now, we are changing that landscape, so of course there will be fractures in the system. So, for example, in Southeast Asian region, our main rollout modes would be through community clinics. And with that said, it means that this clinic does not even have physician or sit-in nurses in the space, which makes it impossible to provide injections.

So, there are a few factors that can contribute to these fractures. The first one would be the infrastructure-dependent delivery. As I said, long-acting PrEP requires a place where injectors, clinical oversight, and monitoring can be done onsite. Secondly is access limitations. So, what PrEP used to be in our region is through community-led clinics, through pharmacies, outreach models to rural settings and those might not be able to accommodate injections. So, we really have to think hard about how can we bring those long-acting innovations to the place where it is needed the most. The third thing is, of course, the shift in control. The next one is, of course, the regional readiness gaps. And the last thing, the most important ones actually is the cost, not only with the drug price, but also the cost of the training, capacity building, different infrastructures, and also policy updates too. So, all of these things combined can prevent people who needed these innovations from getting it.

**David Alain Wohl, MD:**

Yeah, no, that's wonderful. Yeah, I think that's really insightful.

And Landon and Cristina, maybe Landon, you first, any drivers in South Africa that differ or that you want to highlight? And then Cristina, I'm going to ask you the same thing about your experience in Italy.

**Landon Myer, MBChB, PhD:**

The one thing I would want to emphasize is that regarding patient-level barriers, we know from antiretroviral therapy adherence and from treatment compliance studies for decades, providers do a very bad job of predicting who will be adherent. And really, the patient-provider dyad, that joint decision-making is what should really drive the engagement. And so, one of the things we really loathe to do is to put in the hands of providers some adjudication of the social barriers which patients may or may not be able to adhere to long-actings, and to really see that as to give the patients agency in their own treatment decision-making.

**David Alain Wohl, MD:**

Yeah, absolutely. Cristina, what about you in Italy?

**Cristina Mussini, MD:**

In Europe, we are struggling to have reimbursement of these drugs, and because the cost in Europe is evaluated when it's compared to oral PrEP, that is now generic. So, this is a huge problem. But for now, it's not routinely possible to prescribe it. So, this is the major barrier, I think, and we will see in the next future.

**David Alain Wohl, MD:**

Yeah, no, absolutely.

So, as we wrap up over the next couple of minutes, I'm just going to ask each of you just a little bit maybe for pearls or tips about, and I know some of this we've mentioned before, but it even could be based upon your own research or your own experience in clinical practice, but maybe just a clinical tip about PrEP, about initiating, transition monitoring, or even paying for it, as Cristina mentioned, anything that you can share with us that might be a tip for how to make this happen.

So, Cristina, since you have the floor, I'm going to ask you anything that you're doing that might be worthwhile sharing.

**Cristina Mussini, MD:**

I think that what we have seen from the cohort of people on PrEP in Italy is that when you are at the first year, you have 40% risk of discontinuation that increases to 70% after 4 years.

**David Alain Wohl, MD:**

Great. And we heard a lot from Landon already about this, so Fair, I'm going to ask you. Any sort of tips when we think about this that you would share with others in thinking about starting and continuing people on PrEP?

**Jakkrapatara Boonruang, MD:**

If we can instill that resilience or that education into the clients, they can switch back and forth between HIV preventions. So, even if they stop using PrEP, of course they can fall back to condoms. We don't have to forget about condoms, and clients don't need to do that as well. So, I would like to see strategies where we can incorporate resilience into our clients.

**David Alain Wohl, MD:**

Yeah, no, that's wonderful. I really like that. And I think that's a perfect segue to thinking more about patient education. I like what you said. I think today we've talked about who's the optimal patient and how we select those, how we transition the nitty-gritty of the details of the drugs and switching from oral to long-acting, monitoring, including HIV and STIs, and then the challenges of implementing. But I love that you've added on to that this whole idea of, well, but also we need the client to be educated and understand. That's part of that shared decision-making. So, shared decision-making is informed decision-making.

And so, I think patient education tools are really helpful here. And different people have different ones that they've created and some are better than others, but I do help think that there's a usefulness to having something that you can hand to people or go over with people as you talk to them. And so, I think the tools that are available, and there's tools that have been created that I think we can reference here on CME Outfitter's

website that I think could be very useful, and I like that they're graphic because I think people respond visually to graphics more so than just words on paper. So, I think this is, again, another wonderful resource.

And just taking it, again, from the perspective of the person who could benefit from PrEP, here's some insight from a real person who spent time both in Asia and Europe. And as we wrap up, I think this quote brings us home to what we've been talking about. And again, we talk about it in where I work in my clinic. It's a lot of work. You've spent a lot of time here listening to us today, but if everything that you did, all this effort, leads to one person not getting HIV infected, it's all worth it. So, these are things that I think, again, you can take home, think about, implement, and hopefully this would be utilized in a positive way for you and for everyone else.

So, thank you again to our faculty for sharing amazing insights, and thank you to our audience for taking the time out to improve your understanding of PrEP and new PrEP modalities. We encourage you to explore the additional resources that are linked with this activity, continue the conversation in your own practices like we are all the time. We also invite you to visit the CME Outfitters Infectious Disease Hub, which includes free evidence-based resources for both healthcare professionals and for patients. These are tools that are designed to support practical implementation of the concepts that we discussed today, including a status neutral HIV screening and prevention approach.

Now, this activity is part of a broader HIV prevention education series. Additional programs will explore other topics, and we encourage you to explore these programs on your own and build on what we discussed today. So, again, I want to thank all of you. Before we wrap up, just a quick reminder that to receive CME or CE credit, you'll need to complete the post-test and evaluation online. Once completed, you'll be able to download and print your certificate immediately.

Thanks again for your participation and thank you again for international esteemed faculty who've, different time zones and everyone's getting ready for different things but thank you very much for sharing your knowledge and, really, honesty today.

 