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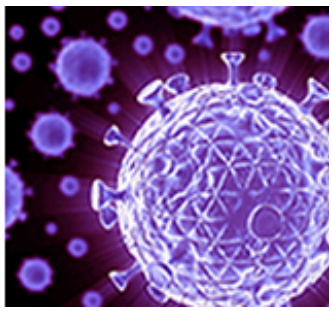

VOLUME 1 — ISSUE 12: TRANSCRIPT

Featured Cases: Emerging Promises and Challenges with the Use of Antiretroviral Therapy for Prevention of HIV Transmission

Our guest author is Kenneth H. Mayer, MD, Professor of Medicine, Harvard Medical School; Director of HIV Prevention Research, Infectious Disease Attending, Beth Israel Deaconess Medical Center; and Medical Director of the Fenway Institute in Boston, Massachusetts.

After participating in this of this activity, the participant will demonstrate the ability to:

- Discuss new findings on the use of antiretroviral agents for primary HIV prevention,
- Describe the impact of early initiation of treatment on HIV transmission, and
- Identify appropriate candidates for pre-exposure prophylaxis for HIV prevention.

This discussion, offered as a downloadable audio file and companion transcript, covers the important issues related to Pre-Exposure Prophylaxis (PrEP) in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 1, Issue 11 *eHIV* newsletter— Emerging Promises and Challenges with the Use of Antiretroviral Therapy for Prevention of HIV Transmission.

MEET THE AUTHOR

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Unlabeled/Unapproved Uses
Dr. Mayer notes that his presentation today will include a discussion of the off-label or unapproved uses of tenofovir gel and maraviroc for HIV prevention.

Faculty Disclosure
Dr. Mayer has disclosed that he has received grants and or research support from Bristol-Myers Squibb, Gilead Pharmaceuticals, and Merck.

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- Clinicians caring for patients with HIV need current information about: appropriate treatment and maintenance of care…guidance for treating comorbidities…and information about emerging findings for treating HIV-associated neurocognitive disorders (HAND)
- The need for more information on HIV topics including updated guidelines for HIV, treating older patients with HIV, managing patients with comorbidities and coinfections, treatment and sequencing strategies for maximizing future therapeutic options, and new and emerging agents for HIV
- Treating comorbidities in patients with HIV, especially among people older than age 50

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MR. BOB BUSKER: Welcome to this *e*HIV Review Podcast.

*e*HIV Review is presented by The Johns Hopkins University School of Medicine. This program is supported by educational grants from Abbott Laboratories, Boehringer Ingelheim Pharmaceuticals, Inc., and Bristol-Myers Squibb.

Today's program is the companion piece to our Volume 1, Issue 11 newsletter topic: *Emerging Promises and Challenges with the Use of Antiretroviral Therapy for Prevention of HIV Transmission*.

Our guest today is that issue's author, Dr. Kenneth Mayer from Harvard Medical School and Beth Israel Deaconess Medical Center in Boston.

This activity has been developed for infectious disease specialists, primary care physicians, nurse practitioners, and other health care practitioners whose practice involves treating patients with HIV.

There are no fees or prerequisites for this activity.

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Learning objectives are, that after participating in this activity, the participant will demonstrate the ability to:

- Discuss new findings on the use of antiretroviral agents for primary HIV prevention;
- Describe the impact of early initiation of treatment on HIV transmission; and
- Identify appropriate candidates for pre-exposure prophylaxis for HIV prevention.

I'm Bob Busker, managing editor of the program. Our guest today is Dr. Kenneth Mayer, professor of medicine at Harvard Medical School, director of HIV Prevention Research at Beth Israel Deaconess Medical Center, and medical research director at the Fenway Institute in Boston.

Dr. Mayer has disclosed that he has received grants and/or research support from Bristol-Myers Squibb, Gilead Pharmaceuticals, and Merck. He has also indicated that his presentation today will include discussion of the unlabeled or unapproved uses of tenofovir gel, as well as maraviroc, for HIV prevention.

Dr. Mayer, welcome to this eHIV Review Podcast.

DR. KENNETH MAYER: Well thank you very much, Bob. It's a pleasure to be here.

MR. BUSKER: In your newsletter issue, doctor, you reviewed the results of several key studies that evaluated the use of pre-exposure prophylaxis — or PrEP — in HIV-uninfected individuals at high-risk. What I'd like to do today is discuss potential application of that data in clinical practice. So if you would, Dr. Mayer, start us out by describing a patient.

DR. MAYER: HM is a 36-year-old HIV infected heterosexual male. He has a CD4 count of 540 cells/cu mm and he is not on antiretroviral therapy at the present time. He has a primary female partner who is HIV uninfected. The couple is in a stable, monogamous relationship and they would like to have children. They present to you to inquire about the best options to protect the female partner from becoming HIV infected.

MR. BUSKER: So this couple is asking about the best options to reduce transmission risk to a potential mother. What kind of counseling would you provide them?

DR. MAYER: As a clinician, you can cite data from two different studies to inform this. There was HPTN 052,[1] which is mentioned in the newsletter, this is the study by Dr. Myron Cohen et al, it was published in the *New England Journal of Medicine* last year. This study looked at heterosexual couples where one partner was HIV infected, the other uninfected and showed that starting treatment early decreased the likelihood of transmitting HIV to the uninfected partner.

There was also the Partners PrEP study,[2] which was following couples where one was infected and the other was uninfected, and in that study the HIV infected partners had high CD4 counts and were not

on treatment at the time, and it was the uninfected partner that used pre-exposure prophylaxis, used tenofovir/FTC or tenofovir alone. And this study showed a decrease in HIV transmission as well. This study was published also in the *New England Journal* also in the past year and the first author was Baeten, and this is also discussed in the newsletter.

The other issues to talk to the patients about are the fact that although they are a stable couple, the question is: are they a monogamous couple? In other words, if the infected partner goes on treatment but the uninfected partner has other partners, that partner may be at risk for acquiring HIV. If the infected partner has other partners, he may acquire sexually transmitted diseases and that can increase susceptibility to HIV from the other partner. So it's not only important to talk about whether the infected partner is interested in going on treatment, or the uninfected partner is interested in PrEP, but it's also important to talk about the nature of the couple's relationship and the risk that outside partners may be having for the relationship.

And then it's also important to talk about the efficacy of barrier protection, because antiretroviral therapy can decrease the risk of infection, but it may not decrease it 100%. And certainly to have children, there has to be unprotected sex, but there may be other times that the couple may be having intercourse where they're not particularly focusing on conception and so continuing to talk about barrier protection is also part of the counseling.

MR. BUSKER: The benefits of initiating treatment early — what are they for the infected partner?

DR. MAYER: In the HPTN 052 study[1] that is cited in the newsletter they found that patients who initiated treatment with CD4 counts between 350 and 550 cells/cu mm were 96% less likely to transmit HIV to their uninfected partners than those who were not on treatment. They also found in that study a modest benefit for the HIV infected person. This study was mainly conducted in the developing world, primarily in Africa, but also in sites in Asia and in Latin America, and there was a pilot site also in the United States and the study found that people who started treatment early were less likely to develop extrapulmonary tuberculosis and other HIV-associated consequences.

Now some people feel that the benefit to the individual from this study is not great for people in the developed world because TB, particularly extrapulmonary TB, is not common. So this is an area of debate. There have been other studies, there was a study called the NA ACCORD study,[3] and this was an observational study throughout North America, and this study looked at people with even higher CD4 counts. So it was not a clinical trial intervention, but looked at people who started treatment at higher CD4 counts — even above 500 and suggested that people who started at higher CD4 counts had decreased morbidity and decreased mortality.

On the other hand, there have been studies from Europe that have not found the same findings and in fact, there is still a study under way now called the START trial[4] that has enrolled patients throughout the world, and this is looking at people with much higher CD4 counts who are asymptomatic and it's not looking at transmission but it's looking at whether there's a clinical benefit. So the clinical benefit is not as definitive as the benefit on transmission when starting at higher CD4 counts, but we do know that from other studies that have been reported over the years such as the Rakai study,[5] published in the *New England Journal* by Dr. Tom Quinn, that starting antiretroviral therapy decreases the amount of virus in the blood, decreases the amount of virus in the genital tract, and that's consistent with decreasing the likelihood of transmission to uninfected partners.

MR. BUSKER: Let's look at it from the other side now — how would you describe the advantages of starting pre-exposure prophylaxis for the uninfected female partner?

DR. MAYER: So pre-exposure prophylaxis for the female partner has been shown to work, particularly in the Partners PrEP study[2] which was the Baeten et al study that is in the newsletter that was published in the *New England Journal*. In that study, women who used PrEP were less likely to become HIV infected, but adherence is extremely important. So another study that was published in the *New England Journal* in the same issue that was referenced in the newsletter by Van Damme, et al, was the FEM PREP study,[6] and that study showed that PrEP did not work for women. And when they went back and looked, the problem was that many of the women were not taking the medicines regularly, as measured by looking at drug levels in the blood. So, many of these women did

not have any detectable tenofovir in their blood, so they were not protected.

So the importance of PrEP for the uninfected partner would be if she's committed to taking a medication on a daily basis to protect herself against HIV. One advantage of PrEP for the uninfected partner would be that if she was not monogamous, if she had other partners and didn't know if they were HIV infected, she would be protected against their HIV as well as her primary partner's HIV. So this may be beneficial.

It really depends on the individual's motivation. In both approaches, either treatment as prevention for the infected partner or PrEP for the uninfected partner, the key issue is medication adherence. So part of the counseling that any clinician would want to do with their patient would be to determine who is really motivated to take the medicine, because that will be the biggest determinant of the success in either case.

There have also been debates about whether it makes sense that if the infected partner starts treatment, does the uninfected partner need PrEP. And there are no definitive studies that prove this one way or another. There is a theoretical benefit and there is some modeling data that says that on a population basis, doing both interventions one might have success. But as a clinician, the most important thing for any clinician is to really get a good sense from both patients who is motivated to take the medication and what's the pattern of their behavior. And very sensitive issues are trying to find out who might be having outside partners because that may be important in terms of figuring out what kind of protection, particularly for the uninfected partner, is necessary, and also then raises the issue about screening for other sexually transmitted infections, as well.

MR. BUSKER: Thank you for that case and that discussion, doctor. Let me ask you now to bring us another patient, if you would, please.

DR. MAYER: RW is a 24-year-old man who has sex with men who reports a recent history of rectal gonorrhea. He reports that most of his partners are males, but he occasionally has female partners. He does not like using condoms because they impair his enjoyment of sex.

MR. BUSKER: With this patient, what would be the first clinical studies you'd perform?

DR. MAYER: The first test that I would do would be an HIV antibody test, but it also would be important for me to get a history of whether he has any flu-like symptoms and when his last exposure to an HIV infected partner might have been. Because somebody who is acutely infected with HIV may have a negative antibody test, and in that case the test that I would want to do would be a plasma HIV RNA test, a viral load test, which will pick up infection before the antibodies turn positive. The antibody test may take weeks to turn positive, particularly if one is using an oral secretion test, one of the rapid tests. The blood test will turn positive sooner but it still can be 10 to 14 days before a positive result may turn up, with even some of the most sensitive antibody tests. So the first question will always be, should I test this person for plasma RNA or is an antibody test sufficient, given his history?

The other important thing to do is to recheck the patient for sexually transmitted infections. Because somebody had rectal gonorrhea once, they may be at risk for that infection again after treatment. This also suggests that they may be having high risk partners, and there are other common sexually transmitted infections that may be asymptomatic that can be easily diagnosed. This would include chlamydia and gonorrhea and chlamydia can be tested rectally and urethrally very easily, urine sample to pick up urethral gonorrhea or chlamydia or a rectal swab and these tests would be using nucleic acid amplification technology. And then to test for syphilis, a simple blood test to test for antibody would be sufficient.

Another thing that I would do would be to check if the patient had a history of hepatitis A and hepatitis B. Hepatitis A I would check for because it is sexually transmitted and it is more common among men who have sex with men, and it's vaccine preventable. Hepatitis B is particularly important to test for because the drugs that are used for pre-exposure prophylaxis against HIV can also treat hepatitis B. And if the drugs are stopped and started intermittently they can cause elevations of the liver function test. Ideally, a person before starting PrEP would either have prior immunity to hepatitis B because of prior infection or would be vaccinated against hepatitis B as well as hepatitis A.

MR. BUSKER: Based on everything you've just said, would you consider this individual a candidate for PrEP?

DR. MAYER: This gentleman is potentially a candidate for PrEP because his behaviors put him at high risk for acquiring HIV. He has had rectal gonorrhea, which means he's had unprotected anal intercourse. He has told the clinician that he does not like using condoms, so those are reasons to think about PrEP. But there are other issues that have to be discussed even before starting PrEP; one of them is what is his motivation for using PrEP once he's told about it, because PrEP is not going to work if he is not adherent. Individuals who are protected with this approach are individuals where there is detectable blood levels of the drugs that are used for PrEP.

So the first thing is to educate the patient about the existence of PrEP to explain what the side effects may be, to explain the importance of adherence, and to determine from him does he think this would be a useful part of a strategy to minimize his risk for HIV infection.

MR. BUSKER: Assuming you and the patient do decide to initiate PrEP, what specific tests would you perform first?

DR. MAYER: The most important thing is to verify that the patient is HIV uninfected. So as previously mentioned, if I thought there was acute HIV infection I would test for HIV RNA, otherwise I would do HIV antibody testing. I would also screen for hepatitis B infection because of the potential risk when stopping and starting with somebody with chronic hepatitis with liver flares. I would certainly screen the patient for sexually transmitted diseases if he had not been recently screened for them. And other important tests to screen for would be the BUN and particularly the creatinine, because the drugs that are used for PrEP, tenofovir and FTC, can cause renal insufficiency and certainly should not be started with anybody with impaired creatinine clearance. And before starting PrEP, I would certainly spend time with the patient talking about the importance of medication adherence, because this pill will not work if it stays in the bottle.

MR. BUSKER: And we'll return, with Dr. Kenneth Mayer from Harvard Medical School, in just a moment.

DR. MICHAEL MELIA: Hello. I'm Michael Melia, associate professor of medicine in the Division of Infectious Diseases and Associate Fellowship Program Director at the Johns Hopkins University School of Medicine. I'm one of the program directors of *e*HIV Review.

*e*HIV Review is a combination newsletter and podcast program delivered by email to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to infectious disease specialists, primary care physicians, nurse practitioners, and other health care practitioners whose work or practice includes treating HIV patients.

Bimonthly podcasts are also available as downloadable transcripts, providing case-based scenarios to help bring that new clinical information into practice in the exam room and at the bedside.

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MR. BUSKER: Welcome back to this eHIV Review podcast. I'm Bob Busker, managing editor of the program. Our guest is Dr. Kenneth Mayer from Harvard Medical School and Beth Israel Deaconess Medical Center. And our topic is the Use of Antiretroviral Therapy for the Prevention of HIV Transmission.

We've been looking at how the information about PrEP that Dr. Mayer reviewed in his newsletter issue might be applied in clinical practice. So to continue in that vein — let me ask you to bring us another patient now, if you would, doctor.

DR. MAYER: SM is a 21-year-old woman who presents to you asking about different ways she can protect herself against HIV. She's in a stable monogamous relationship but believes that her partner is not faithful. She has had a trichomonas infection in the last six months, but has not seen any other partners.

MR. BUSKER: An interesting situation, Doctor. How would you counsel her about HIV prevention?

DR. MAYER: In this case, the challenge is trying to understand the risks that the partner has because her individual risk is not particularly high, she's in a monogamous relationship. But if her partner is HIV infected, she would be at high risk for acquiring HIV. So the art of medicine here would be to inquire about the feasibility about her having her partner come in for screening in order to ascertain her true risk. Because she had developed trichomonas once in the last six months, it would certainly be important to screen her for other sexually transmitted infections, because trichomonas implies that her partner had acquired this from another partner. So I would screen her for syphilis, for gonorrhea and for chlamydia, and the gonorrhea and chlamydia tests would depend on where she indicated she was having sexual intercourse. So if she indicated she was only engaging in vaginal intercourse, I would only screen there, but I would also ask about whether she had had any anal intercourse, herself. I would also ask this woman, because she's young, about whether she had been vaccinated against human papillomavirus. The data are very strong that certainly if she is in her early 20s and she has not received this vaccine, she's still a candidate for the vaccine and this will protect her against four different types of HPV.

MR. BUSKER: What about pre-exposure prophylaxis? Would you consider her a candidate?

DR. MAYER: We don't have sufficient data yet to really know whether she is a candidate for PrEP. We really want to get the data about her partner to know about her risk. If the partner can come in and be tested for HIV and he's found to be HIV infected, she would definitely be a good candidate for PrEP, providing that she was motivated to be adherent, because several studies have shown that women can benefit from oral pre-exposure prophylaxis. The Partners PREP study revealed this and this was the Baeten et al study[2] in the *New England Journal*, and the other study was the TDF2 study[7] conducted by the Centers for Disease Control in prevention in Botswana. And this paper was led by Dr. Thigpen and this was also published in the *New England Journal* in the same issue as the Partners PrEP study.

But as previously noted, there were studies that have not shown the benefit of PrEP for women and in these studies adherence was the key issue. So if the partner was found to be HIV infected, the next question would be whether the woman was motivated to take a medication on a daily basis because that's the only way that PrEP has been shown to be effective.

On the other hand, if she's not having other partners and if her partner tested HIV negative, then it would be really important to get more history from the uninfected male partner to ascertain whether he was at increased risk for inquiring HIV and could introduce it into the relationship. If his pattern of behavior was not of significant risk for acquiring HIV, then she would not be a candidate for PrEP.

MR. BUSKER: I want to bring up something it's likely many clinicians have encountered: let's say this woman has read a news article or found something on the Internet, and she asks you about a topical HIV protection she might be able to use. How would you respond?

DR. MAYER: There's been a lot of interest in microbicides which are topical gels that could potentially protect women and potentially men against HIV. However, none of these are approved by the Food and Drug Administration. There has been one study, the CAPRISA 004 study,[8] conducted in South Africa that showed that a gel that contained tenofovir was protective. This study was published in *Science* in the summer of 2010. Subsequent studies have not confirmed the efficacy of this approach and once again, adherence may be a concern. There are further studies under way to see whether adherence can be enhanced and whether this is a valid approach. But at the present time there no approved microbicide gel so the patient should be commended for keeping up on the literature and paying attention to the issues, but should be told that at the present time the only way to use antiviral medication to protect her against HIV would be to use oral medication, and that would be oral pre-exposure prophylaxis.

MR. BUSKER: What about reinforcing the benefit of condoms for this patient?

DR. MAYER: Condoms are extremely important for HIV protection. The problem is that some people don't like using them. But it is clear that if providers can remind people about the benefits of condoms, that they are an important part of the successful HIV prevention strategy.

MR. BUSKER: Doctor, thank you for discussing those cases with us. Let me change direction on you now and ask you to look to the future for us: what's currently under investigation regarding pre-exposure prophylaxis?

DR. MAYER: At the present time we only have one compound that is approved by the Food and Drug Administration to be used for oral pre-exposure prophylaxis. That's the combined medication tenofovir and emtricitabine that are co-formulated into a single pill which should be taken on a daily basis. However, there's a bunch of new studies under way to try to see whether this approach, pre-exposure prophylaxis, can be simpler and whether other medications or other modes of delivery can be used.

So to simplify the regimen, there are studies now trying to look at using the medication only around the time that people are having sex, so those studies are under way now. So that would allow people to be more selective in their pattern of pill use if they're not having unprotected sex on a daily basis. We do not know whether that approach will be successful yet and these studies are still under way, but they may provide some important insights that may make it easier for people to use the existing medication.

There are also studies looking at other antiretroviral drugs. So, one of the studies is looking at the compound maraviroc, which is an entry inhibitor, and to see whether it by itself or in combination with other antiretrovirals might be useful for pre-exposure prophylaxis. That is an expanded safety study, so it will still be years before we know whether this approach has comparable efficacy to the one approach that is approved by the FDA.

In addition, there are now studies looking at whether antiviral compounds can be put in vaginal rings, in which case a woman might insert a ring once a month so that gets around the issue of daily adherence. And there are studies just beginning now to look whether newer antiretrovirals can be given as injectable medication. So the field is starting to look like hormonal contraception — in other words, one size may not fit all.

But we are at a point right now where only one approach has been shown to be effective. So the one thing that we can recommend for patients who may be at risk for HIV would be oral daily medication using tenofovir/emtricitabine, but in the future, there may be other opportunities to offer different modes of prevention for appropriate populations.

For those individuals, both providers as well as patients, who are really interested in this whole field of antiretroviral medication for HIV prevention, there are a number of web resources and the one that I like to look at often is from the AIDS Vaccine Advocacy Coalition,[9] they are called AVAC, and their website is www.avac.org. So they keep a list of the current trials and the current results about this whole approach of using antiretroviral medication for prevention.

MR. BUSKER: Thank you for sharing those thoughts, doctor. To wrap things up, let's review today's discussion as it applies to our learning objectives. So to begin: new findings on the use of antiretroviral agents for the prevention of primary HIV.

DR. MAYER: Today we discussed the use of antiretrovirals as pre-exposure prophylaxis. So this means that HIV uninfected people would be using the medication so they do not become HIV infected. We talked about several different studies today, we talked about the iPrEx Study[10] which focuses on men who have sex with men, which is Grant, et al, in the *New England Journal*, and we talked about the Partners PrEP study[2] which focuses on heterosexual discordant couples as well as the Botswana PREP study,[7] which focused on young adults.

MR. BUSKER: And the key take-home messages from these studies?

DR. MAYER: It is extremely important for clinicians to assess their patients' risks. This means talking to them about their sexual behavior, because not everybody is an appropriate candidate for PrEP. The other key take home is that PrEP will not work if people are not adherent. So once there is an initial conversation about PrEP, it's very important to ascertain whether individuals want to take it on a daily basis and are willing to follow that regimen. And then the third issue is that before PrEP is initiated, because it is a biomedical intervention, there are a variety of screening tests that need to be done, including screening for renal function, screening for hepatitis B status, and very important, to screen for sexually transmitted diseases and to be sure that a patient is not infected.

MR. BUSKER: And our second objective: the impact of early initiation of treatment on HIV transmission.

DR. MAYER: We discussed today the HPTN 052 study,[1] which followed HIV-discordant couples and showed that earlier initiation of treatment decreased the likelihood of transmission to the uninfected partner by 96%. When we're talking about early treatment as prevention, we're talking about individuals who otherwise feel quite well, so it's very important for them to understand the benefits that they may have from starting treatment early, which are some personal benefits, decreasing rates of certain illnesses that they may be at risk for, but particularly making them less infectious to their partners. However, this means that they have to commit now to starting antiretroviral therapy with three medications for the rest of their lives. So ascertaining whether the individual is really ready to commit to begin treatment and to be adherent to treatment is a very important part of the process before initiating antiretroviral treatment in these individuals.

MR. BUSKER: And that leads right into our third learning objective: identifying appropriate candidates for pre-exposure prophylaxis.

DR. MAYER: Today we discussed the fact that not everybody is a candidate for pre-exposure prophylaxis. The important thing is for the clinician to talk to the patient about his or her sex life and to determine whether somebody has engaged in intercourse on an ongoing basis with a known infected partner, and that would certainly be an indication for initiating pre-exposure prophylaxis. The other population of individuals who might benefit from pre-exposure prophylaxis are people who are engaging in recurrent high-risk behavior even if they don't know the status of their partner. So these may be individuals who have anonymous partners or who have multiple partners, and these are particularly people who come in with recurrent sexually transmitted infections.

In the setting of some individuals, such as women who may have a partner where they think their partner may be at high risk, it is very important for the clinician to try to bring in the partner because not all partners are equally high risk, and this will help determine whether that female patient may benefit from PrEP or whether counseling of the couple may be a more useful intervention than initiating antiretroviral therapy for an HIV uninfected person.

MR. BUSKER: Dr. Kenneth Mayer, from the Harvard Medical School, Beth Israel Deaconess Medical Center, and the Fenway Institute, thank you for participating in this eHIV Review Podcast.

DR. MAYER: Bob, thank you so much, I very much enjoyed speaking with you today.

MR. BUSKER: This podcast is presented in conjunction with the eHIV Review Newsletter, a peer-reviewed literature review certified for CME credit, emailed monthly to clinicians treating patients with HIV.

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Thank you for listening.

REFERENCES

1. Cohen MS, Chen YQ, McCauley M, et al; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med.* 2011;365(6):493-505.
2. Baeten JM, Donnell D, Ndase P, et al; Partners PrEP Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med.* 2012;367(5):399-410.
3. Kitahata M, Gange S, et al; Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival. *N Engl J Med*. 2009;360:1815-1826.
4. Strategic Timing of Anti-Retroviral Treatment. National Institute for Allergy and Infectious Diseases.
5. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med.* 2000 Mar 30;342(13):921-929.
6. Van Damme L, Corneli A, Ahmed K, et al; FEM-PrEP Study Group. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med.* 2012; 367(5):411-422.
7. Thigpen MC, Kebaabetswe PM, Paxton LA, et al; TDF2 Study Group. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med.* 2012;367(5):423-434.
8. Abdool Karim Q, Abdool Karim SS, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010 Sep 3;329(5996):1168-74. doi: 10.1126/science.1193748. Epub 2010 Jul 19.
9. AIDS Vaccine Advocacy Coalition (AVAC) Web site. http://avac.org/
10. Grant RM, Lama JR, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *Engl J Med.* 2010 Dec 30;363(27):2587-99. doi: 10.1056/NEJMoa1011205. Epub 2010 Nov 23.