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Pre-Exposure Prophylaxis (PrEP)-Associated HIV Monitoring and Self-Testing

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Guest: Dr. Yusheng Zhu is a Professor and Vice Chair for Academic Affairs in the Department of Pathology & Laboratory Medicine and Adjunct Professor of Molecular and Precision Medicine at the Penn State College of Medicine, Hershey, Pennsylvania.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Despite substantial progress in the diagnosis and treatment of HIV, it remains a significant global health problem with an estimated 40 million individuals infected worldwide in 2023.

The World Health Organization has set an ambitious goal of ending the AIDS epidemic by 2030, and a central pillar of this campaign is for 95% of HIV-infected individuals to know their status and for 95% of those who know their status to be receiving treatment. While several highly effective treatment options are available, an even better strategy is to prevent infection in the first place. The first FDA-approved medication for pre-exposure prophylaxis, or PrEP, was released in 2012, and several others have followed in the intervening years. While these medications reduce the risk of HIV transmission, they require documentation of a negative HIV test, which represents a barrier for some patients.

A review article in the April 2026 issue of *Clinical Chemistry* describes a strategy to increase PrEP uptake by making it easier to document one's HIV negative status: at home self-testing. Today, we'll chat with the article's author. Dr. Yusheng Zhu is Professor and Vice Chair for Academic Affairs in the Department of Pathology and Laboratory Medicine and Adjunct Professor of Molecular and Precision Medicine at Penn State College of Medicine, Hershey, Pennsylvania. So, Dr. Zhu, your paper discusses pre-exposure prophylaxis, or PrEP-, associated HIV monitoring and self-testing. For those who may not be familiar with PrEP, just give us the basics, tell us some of that background.

Yusheng Zhu: Absolutely, Bob. First, I would like to thank my collaborator, Dr. Jarrett Sell, for his great contributions to this paper. Most people may know HIV post-exposure prophylaxis, or PEP, which is to use antiretroviral medications in an emergency to prevent HIV infection within 72 hours of potential HIV exposure. For example, a needle stick injury. Unlike PEP, where individuals only need to take the medications for 28 days, pre-exposure prophylaxis, or PrEP, requires daily or

regular long-term utilization of antiretroviral medications to prevent HIV acquisition in people without HIV, but who are at risk. PrEP is very effective, which can significantly reduce the risk of HIV infection if people take the medications as prescribed.

Bob Barrett: And what are the currently available HIV PrEP medications and how do they work?

Yusheng Zhu: Sure. Currently available HIV PrEP medications utilize the same mechanisms of action as the medication developed for the HIV treatment. For example, TDF/FTC is a combination of two nucleoside reverse transcriptase inhibitors, NRTIs, that terminate HIV DNA chain elongation. TAF/FTC is another NRTI combination. These medications are highly effective, but require daily oral administration, which may be inconvenient for some people, causing non-adherence. To improve patient compliance, injectable long-acting medications for HIV PrEP have been developed and they are currently available. For example, cabotegravir is the first FDA-approved injectable medication for HIV PrEP. It is an integrase strand transfer inhibitor that blocks the integration of the double-stranded HIV DNA formed by reverse transcription into the host DNA during the integrase strand transfer step. Individuals only need an injection every month for the first two months, then one time every two months. In June 2025, the FDA approved lenacapavir, an HIV-1 capsid inhibitor as an injectable medication administered every six months for HIV PrEP.

Bob Barrett: And tell us what roles do clinical laboratorians play in the HIV PrEP program?

Yusheng Zhu: Clinical laboratorians play a critical role in HIV PrEP. We perform initial HIV screening and confirmation tests to ensure people are HIV negative before starting PrEP. Currently most clinical laboratories use HIV-1/2 antigen antibody immunoassays for screening with a reflex HIV-1/2 antigen antibody differentiation assay for confirmation within one week of initiating PrEP. We may also perform HIV RNA test for patients with suspected acute HIV infection, or high-risk recent unprotected sexual exposure. In addition, the clinical laboratories perform several other tests including eGFR, lipids, and sexually transmitted infections such as gonorrhea, chlamydia, and syphilis at the baseline and for ongoing monitoring while on treatment with HIV PrEP with regular frequencies.

Bob Barrett: Dr. Zhu, in your article, you discuss HIV self-testing for PrEP, why is this important?

Yusheng Zhu: That is a great question. Clinical laboratory-performed HIV tests are quite sensitive and specific for HIV screening and

diagnosis. However, there are disadvantages to laboratory-performed tests including a lack of patient privacy. The patient must go to a healthcare facility for blood collection and a longer turnaround time for test results compared with self-testing. HIV self-testing makes it easier for individuals to learn their HIV status because it can reduce the fear of stigma and discrimination.

As a discreet, convenient, and empowering approach, HIV self-testing is more accessible than laboratory testing, since it limits many well-documented barriers to laboratory diagnosis for HIV, including long waiting times, inconvenient specimen collection, and fear of lack of confidentiality.

In some countries or regions, the lab-performed fourth generation HIV-1/2 antigen antibody assays are unavailable. In this case, HIV self-testing can be used in PrEP. The WHO encourages the use of rapid HIV tests for self-testing because it is well-known that provider administered testing could limit PrEP uptake. I should point out that oral HIV self-testing is not recommended due to the low sensitivity of this test for diagnosing recent HIV infection. In the United States, the FDA has not approved any HIV self-tests specifically for PrEP.

Bob Barrett: So, does HIV self-testing for PrEP have any limitations?

Yusheng Zhu: Yes. Currently available HIV self-testing methods rely on antibody assays. These assays could miss a significant portion of asymptomatic HIV carriers during the two to four weeks of the window period, which is the time from acquisition of HIV until a test can detect the infection. The possible alternative is to use nucleic acid testing, which is the most sensitive method for identifying the presence of HIV as early as 10 days after acquisition of HIV. But this is more expensive and complicated laboratory-performed test with a longer turnaround time. It is not available in resource limited settings.

Bob Barrett: Well, finally, Dr. Zhu, let's look ahead. Where is your research in this field going in the future?

Yusheng Zhu: I have been working with my collaborators to develop and validate HIV molecular diagnostics devices and assays that can be potentially used in HIV PrEP. For example, reverse-transcription loop-mediated isothermal amplification, or RT-LAMP, is an amplification method that enables rapid and sensitive detection of specific HIV RNA. RT-LAMP does not require a thermocycler but maintains a comparable level of specificity and sensitivity to PCR tests. A compact point-of-care testing device for semi-quantification of HIV RNA has been developed. The device streamlines plasma separation, viral RNA extraction and real time RT-LAMP with built-in

internal references for semi-quantification. Only 100 microliters of whole blood is needed.

A smartphone-based interface is used for real time monitoring of viral RNA. Compared with clinically tested samples, this device demonstrates 95% accuracy. This device could serve as a starting point for providing rapid, easy to use and cost-effective HIV RNA self-testing solutions. We are going to conduct further validations and clinical trials to evaluate the performance of this novel device and method for HIV self-testing.

Bob Barrett: That was Dr. Yusheng Zhu from Penn State College of Medicine in Hershey, Pennsylvania. He wrote a review article in the April 2026 issue of *Clinical Chemistry* summarizing HIV self-testing in pre-exposure prophylaxis. He's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.