Preexposure Prophylaxis in the United States: An Evolving HIV Prevention Opportunity

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(See the Major Article by Wu et al on pages 144–9.)

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Remarkable progress in preventing new human immunodeficiency virus (HIV) infections has occurred during the past few years. That progress is principally measured by the accelerated rate at which biomedical interventions are being implemented, a trend that promises to greatly impact the HIV epidemic into the future. The first intervention, preexposure prophylaxis (PrEP), is the topic of an article in this issue of Clinical Infectious Diseases. The other powerful biomedical intervention, dubbed “treatment as prevention,” has been around for years, initially in prevention of maternal-to-child transmission, but now is supported by stronger proof of effectiveness [1]. Along with measures such as expanded routine HIV testing, postexposure prophylaxis (PEP), and safer sexual and injection drug use practices, a long-awaited decrease in new HIV transmissions has become more possible than any time in the history of HIV since the dramatic declines that followed the adaptation to safer sexual practices much earlier in the epidemic.

The study by Wu et al [2], in this issue of CID, provides a look at the uptake of PrEP into practice as reflected by the increase in prescriptions of co-formulated tenofovir disoproxil fumarate (TDF)/emtricitabine (Truvada) for PrEP. The study measured claims data from an extremely large employer-sponsored health insurance database. Although studies looking at billing claims data are imperfect measures of overall clinical use and the population studied is covered by private health insurance plans, the authors do account for the most important variables and confounders. The study design could not account for prescribing changes that might have occurred when the individual carriers added PrEP as an indication for TDF/emtricitabine to their approved formularies. In addition, the current study does not assess uptake among the various racial and ethnic groups in which uptake has been slow. Nevertheless, this study allows the reader a view of the principal findings: a dramatic uptake in PrEP usage in 2014, and few PrEP prescriptions for women. The nearly identical increase in uptake during 2014, at the Kaiser system in San Francisco [3] and among Medicaid recipients in New York [4], provides additional support for the first finding.

The time frame for the study (2010–2014) spans most of the short history of PrEP, from the first major clinical trial in December 2010 [5] through the 2012 US Food and Drug Administration approval of TDF/emtricitabine for PrEP and the 2014 revised Centers for Disease Control and Prevention (CDC) PrEP guidelines [6]. It is not surprising that the spike in uptake was not until 2014, when the usual factors that produce acceptance of a new intervention were in place. For clinicians, those factors included sufficient clinical trials results supporting the effectiveness of PrEP; reports of real-world experience confirming PrEP as an accepted prevention tool; approval of the drug for the specific indication; and national guidelines spelling out indications, laboratory monitoring protocols, treatment approaches, and follow-up schedules. Perhaps equally important as clinician acceptance was patient acceptance. Prior to 2014, concerns surrounding the appropriate place for PrEP as an adjunctive or even a sole prevention strategy had been percolating, especially within the community of men who have sex with men (MSM). The controversy, as well as the anticipation, was considerable. Issues such as effectiveness, safety, appropriateness as a prevention measure, cost, and coverage were dissected. Among the most divisive issues was concern about risk compensation (increase in unsafe sexual activities accompanying the sense of PrEP-related protection). The prolonged dialogue, however, raised awareness of this new intervention, especially among MSM. This probably is reflected in the claims data results, which showed that when PrEP prescribing took off, fully 97.5% of prescriptions were for men. The small proportion of PrEP prescriptions for women almost certainly reflects that such a community dialogue and “vetting” of PrEP as a viable prevention measure did not exist among women as it did among MSM.
Additional studies and further experience with PrEP in various clinical settings have given a fuller picture of PrEP. In general, PrEP is associated with low rates of HIV transmission and only modest side effects and adverse consequences. The “real world” rate of HIV transmission appears to be lower than the rate seen in many clinical studies, as adherence appears to be greater outside of the clinical trial milieu. With adherence, PrEP success rates at or above 90% reduction in transmission are expected. The most important side effects, TDF-induced renal function impairment and bone mineral density loss, were anticipated in the guidelines. Renal side effects (decreased creatinine clearance and proteinuria) generally have not heralded more serious problems, so guideline recommendations to monitor renal function and to avoid using TDF/emtricitabine in patients with creatinine clearance <60 mL/minute remain. The significance of bone mineral density loss has not been clinically determined [7]. In addition, 2 anticipated adverse consequences have now been better characterized: Risk compensation, with an increase in condomless sexual practices, has been reported [3,8] but is difficult to assess. Reports indeed show that although HIV transmissions are rare during PrEP usage, very large numbers of PrEP users admit to unsafe sexual practices and acquire sexually transmitted infections (STIs). But it is not clear whether this represents risk compensation or other factors such as the baseline high levels of at-risk activity among the PrEP-using population or the detection of STIs as part of the PrEP routine follow-up testing schedule. For the clinician, knowing that so many persons taking PrEP acquire STIs is a powerful reminder to provide frequent risk reduction counseling, regular laboratory monitoring for STIs (perhaps more frequently than the recommended 6-month intervals) and emphasizing the importance of follow-up. Finally, the degree to which transmission of drug-resistant HIV during PrEP treatment can occur is still being evaluated. Nevertheless, testing patients for HIV before and during courses of PrEP remains critically important.

Now that PrEP is more firmly established as a key prevention tool, the question of who should be providing PrEP has been raised [9]. As a primary care family physician, it is clear to me that any clinician caring for patients with HIV or at risk for acquiring HIV needs to be active in charting a successful prevention course. Providing primary PrEP care means more than prescribing and monitoring for drug toxicities. Ongoing engagement in care with follow-up monitoring for HIV infection and STIs, providing risk reduction counseling, and educating patients about consistent use of PrEP are critical. Guidelines and standard protocols for laboratory monitoring and prescribing PrEP are available [6] and consultative help on indications and implementation of PrEP is readily available for clinicians via our national free PrEPline at 1-855-448-7737. In addition, infectious disease physicians, HIV experts, primary care clinicians, and emergency department clinicians who are called upon to assess the need for PEP after sexual exposure should be mindful that sexual exposures are often double prevention opportunities: first, averting transmission from the immediate exposure with PEP; and second, alerting the patient and primary care clinician that those patients with ongoing risk will be candidates for PrEP in the future [10]. On our national PEPline (1-888-448-4911) we routinely remind and advise the “PEP clinician” how to discuss PrEP with those patients at ongoing risk and how to initiate PrEP following completion of the 30-day PEP course (“PEP to PrEP”).

Notes
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