

Pre-Exposure Prophylaxis for HIV Can It Be Implemented in the Real World?

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In July of 2012, the U.S. Food and Drug Administration (FDA) approved emtricitabine/tenofovir disoproxil fumarate (Truvada) to reduce the risk of sexual transmission of HIV among uninfected individuals at high risk of infection. The approval for pre-exposure prophylaxis (PrEP) was based on two large, randomized, double-blind, placebo-controlled trials, one in HIV-negative men and transgender women who have sex with men, and one in heterosexual HIV-discordant couples.^{1,2}

In general, FDA approval is followed relatively quickly by increased use of that medication. This is especially true when there are no other medications available and the approval process was based on randomized, blinded, placebo-controlled trials, as it was with PrEP. However, for a wide variety of reasons, diffusion of PrEP into clinical practice, which the authors of one article in this supplement to the *American Journal of Preventive Medicine* characterize as “a wicked problem,”³ is not likely to occur easily.

There are a number of reasons why diffusion of PrEP into clinical practice might occur slowly. PrEP falls into the familiar and challenging category of treating for prevention. For sure, it is always difficult to motivate people to take medications to prevent conditions because they do not receive immediate benefits in the sense of feeling better. Recommending daily PrEP to individuals at risk for HIV seroconversion is similar to recommending anti-hypertensive medications because of the risk for stroke and other vascular complications. The need is there, but adherence to treatments that do not bring symptomatic improvement is notoriously poor.⁴

For both patient and clinician, the decision to initiate PrEP is even more complicated than the decision to prescribe anti-hypertensive medications. HIV-negative people may be reluctant to mention to their provider that they are having unsafe sex. In instances when a patient comes for treatment or follow-up of a sexually transmitted disease, which is evidence of high-risk unsafe sex, discussion of future prevention measures often follows. But in other cases without an index infection to discuss,

only a frank discussion between a nonjudgmental healthcare provider and a forthcoming patient in the course of routine healthcare maintenance will reveal that the patient is having unsafe sex. Following an assessment of at-risk activities, an equally challenging discussion needs to occur to address whether the person can stay safe in the future through the consistent use of condoms and/or avoiding certain sexual practices or whether the person needs to also take PrEP. Unfortunately, many people do not have a healthcare provider with whom they can have such a frank discussion. Without this important conversation, a critical prevention opportunity is lost, whether the patient chooses PrEP or not.

The process of obtaining PrEP medications and monitoring PrEP use will be challenging as well. For patients who choose to take PrEP who have private insurance, coverage might be problematic. It is not certain whether all insurance companies will pay for the medication or whether clinicians might need to obtain special authorization for coverage of PrEP medications. In the absence of insurance coverage, patients will, at a minimum, need a provider who is willing to submit the forms necessary to obtain medication through the company's patient assistance program (www.gilead.com/truvada_assistance_program). Even so, patients will need to have insurance or be able to self-pay for their every-3-month visits and laboratory evaluations to confirm they have not seroconverted and are not having medication side effects.

For low-income patients, especially those who are uninsured or publicly insured by Medicaid, arranging for PrEP, which is not simple under the best of circumstances, can become dramatically more difficult. This is an especially important issue because low-income people and those of color are more likely to become infected.^{5,6} Unfortunately, whether they are uninsured or have Medicaid, low-income individuals also are less likely to have a primary care clinician than people of higher income. If they are uninsured, even if they can obtain medications through a patient assistance program, they may not be able to afford physician visits and drug monitoring and might have serious challenges in simply getting to routine visits. These factors provide substantial problems for safe PrEP treatment.

For patients on Medicaid, each state program determines its own formulary for fee-for-service providers. For patients for whom care is provided through a man-

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aged care plan, the plan determines whether to cover the medication. If a patient is on Medicaid, and the program does not cover Truvada for PrEP, Gilead has committed to covering the medicine through their patient assistance program.

Realistically, for low-income people to receive PrEP, a government agency or a private nonprofit agency would need to create a specific program, with providers trained to provide this service in time-efficient ways. Indeed, as discussed in this supplement, this model has been used successfully to facilitate access to post-exposure prophylaxis⁷ and buprenorphine.⁸ While successful, programs in both these areas have had challenges in educating patients and providers about the services, obtaining reimbursement for the costs of the program, and diffusing the model to a broad group of providers.

Because public health programs are always underfunded for their mission, creating PrEP programs will raise complicated resource allocation issues. Since it is unlikely that there will be new federal funding streams to create PrEP programs, local governments and nonprofit agencies will need to determine whether to divert funds to PrEP. Ideally, public systems would make resource allocation decisions on the basis of how to get the best (health) bang for the buck. Health can be reasonably operationalized as quality adjusted years of life per dollar. It is hard to know exactly where PrEP falls in the spectrum of health benefits derived from different expenditures. Although PrEP is ideally an adjunct to, as opposed to a substitute for, other prevention measures, comparative cost data will be important. Better information about the costs and benefits of PrEP in a real-world setting, as well as the costs and benefits of other commonly prescribed interventions, will be required.

But the reality is that the decisions on what services to cover in public systems are not made by a purely analytic weighing of the costs of different treatments per unit of benefit. If that were the case, we would provide methadone treatment to every heroin or opiate user who wished to quit, by diverting money from chemotherapy for patients with incurable malignant disease. But decisions of what to cover and what not to cover in public systems are much more complicated and more heavily affected by community practice, public demand, availability of clinicians and other resources, medical school affiliations, and political considerations, as well as bias toward treating more advanced disease over prevention.

For several reasons, it may be difficult to convince policy leaders to divert funding to PrEP. For one thing, many patients who might benefit from PrEP do not know about it, and even if they did, might not place HIV acquisition high on the list of things they are worried about

because they are busy working to support themselves, their families, or their drug habits. In addition, policy-makers and philanthropists who ordinarily support prevention efforts might well feel that low-income uninsured individuals have another way of avoiding HIV infection (i.e., safer sex) and therefore PrEP should be a lower priority.

Although it will be difficult, the decision for creating public programs for low-income people to obtain PrEP should be based on a thoughtful resource-allocation process. There is great value in treating those at high risk for seroconversion: In addition to saving them from future morbidity and healthcare expense, each infection prevented is one less person who can transmit the infection to others. Finding ways to make PrEP available for low-income people is important to prevent the ultimate irony: that PrEP increases the disparity in infection rates between lower- and higher-income people because only those with the higher income can afford the treatment.

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