EDITORIAL COMMENTARY

Scaling Up Antiretroviral Preexposure Prophylaxis: Moving From Trials to Implementation

Kenneth H. Mayer[1,2,3] and Douglas S. Krakower[1,2,3]

[1]The Fenway Institute–Fenway Health, [2]Beth Israel Deaconess Medical Center, and [3]Harvard Medical School, Boston, Massachusetts

(See the Viewpoints HIV/AIDS by Kelley et al on pages 1590–7.)

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During the past decade there have been 10 efficacy trials evaluating the use of oral or topical tenofovir-based regimens to prevent human immunodeficiency virus (HIV) transmission in at-risk populations, including young African heterosexuals, men and transgender women who have sex with men, and Thai injecting drug users [1–10]. Seven of these 10 studies demonstrated the efficacy of antiretroviral preexposure prophylaxis (PrEP), and in 3 studies where HIV incidence did not differ between the intervention and control arms, the major reason for the lack of efficacy was medication nonadherence [7, 8, 11].

The weight of the evidence from these PrEP studies has led to US Food and Drug Administration approval for the use of oral tenofovir coformulated with emtricitabine for anti-HIV PrEP [12]. Demonstration projects are underway in several parts of the world, so it is likely that tenofovir- emtricitabine for PrEP will soon be approved for use in several countries in Latin America, Africa, Asia, and Europe [13]. Of note, the 3 studies focusing on men who have sex with men (MSM) had highly successful results, including the PROUD (Pragmatic Open-Label Randomised Trial of Preexposure Prophylaxis) study in the United Kingdom, in which MSM who attended genitourinary medicine clinics were randomized to receive PrEP immediately or be put on a waiting list and be offered PrEP after a year. The HIV incidence was so high in the waiting list group (7.8% annually), and PrEP so effective (86% decrease in HIV acquisition), that the study had to stop early, after accrual of about 10% of projected enrollment. These findings are particularly important, given that the rate of new HIV infections continue to increase dramatically among MSM domestically and globally.

Despite the demonstrated efficacy of PrEP and the approval by regulatory bodies in the United States, uptake has not been rapid. In recent years, the concept of a continuum of HIV care has been a helpful heuristic for the assessment of the effectiveness of virological suppression at a population level [14]. In the current issue of *Clinical Infectious Diseases*, Kelley et al [15] have reviewed some of the sources of attenuation in the Atlanta HIV prevention continuum (ie, barriers to PrEP provision for high-risk MSM). Their data suggest that only about 15% of MSM who would be appropriate candidates for PrEP would probably access the medication. Part of the problem is that PrEP awareness remains low, albeit having increased somewhat over the past few years [16, 17]. Social disenfranchisement plays a role; that is, MSM who are poorer or less educated seem to be less informed about PrEP [18]. Medical mistrust remains entrenched for some African Americans because of historical adverse experiences with clinical research (eg, the Tuskegee experiment), leading to the tuning out of new information [19]. Media campaigns by some "PrEP denialists" may have created confusion for some who might benefit from PrEP [20].

In addition to lack of awareness and misinformation that may lead to reticence about using PrEP, another major barrier is posed by medication and health services costs (>$12 000 annually for those without insurance). The current study by Kelley et al [15] highlights this challenge in the current health reform environment. Because Atlanta is a "blue" city in a "red" state, Georgia government has not embraced the Affordable Care Act, leaving many who might benefit from PrEP to be either uninsured or underinsured. Because 20 US states have not expanded Medicaid, access to PrEP may

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Correspondence: Kenneth H. Mayer, MD, The Fenway Institute–Fenway Health, 1340 Boylston St, Eighth Flr, Boston, MA 02215 (khmayer@gmail.com).

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be challenging for some living in urban areas of high HIV prevalence, such as Miami, Dallas, Houston, and New Orleans. Awareness and use of PrEP and postexposure prophylaxis seem to be lower among MSM who live in states with more stigmatizing environments [21]. Although the manufacturer of tenofovir-emtricitabine, Gilead Sciences, has a drug assistance program [22], many individuals may fall between the cracks by having incomes that are too high and/or by insurance plans with onerous copayments.

Because PrEP is a biomedical intervention, accessing it requires either an informed consumer or a busy clinician taking the time to determine whether a patient might benefit from PrEP. Primary providers generally do not routinely ask about sexual orientation or behavior [23, 24], so many opportunities to initiate PrEP may be missed. Moreover, patients may be uncomfortable to request PrEP, anticipating moralistic conversations if they disclose their sexual orientation [25] and preference for condomless sex. There is no consensus among clinicians about who should provide PrEP. Some would argue that primary care providers are ideal, because sexual health promotion should be an intimate part of primary care, but many feel they are not equipped to discuss the nuances of sexual behavior [26] and are not familiar with prescribing antiretroviral medication [27]. Conversely, infectious disease specialists who might only provide primary care for persons living with HIV may not be comfortable in managing otherwise healthy patients who request prophylaxis because of behavioral risks. Some attempts to address clinician time constraints include the development of algorithms using a limited number of specified questions to generate a risk score to determine whether a patient might be an appropriate candidate for PrEP [28]. The use of electronic technologies whereby patients can self-report their behavioral risks, either at home or in waiting rooms, could also save time and allow clinicians to routinely determine whether a patient's recent behavioral patterns might merit a discussion about PrEP.

Despite all these impediments, the use of PrEP by MSM seems to be increasing in some quarters. In San Francisco, it is estimated that >10% of at-risk HIV-uninfected MSM have used PrEP, but behavioral surveys suggest that many more could benefit [29]. At Fenway Health, a Boston community health center with a specialization in sexual and gender minority health, PrEP prescriptions have increased in recent years, with >500 being started in the past year [30]. What San Francisco and Boston share in common is an environment that has supported civil equality for sexual and gender minorities, early implementation of health reform, and access to culturally tailored behavioral health programs. It would be unfortunate if the uptake of PrEP was limited to a few "blue islands," when it is clear that individuals who might benefit from PrEP are found in diverse geographic settings. Some of the impediments to wider PrEP use should be readily overcome by using new technological tools to disseminate information, increasing the health literacy of at-risk persons and enhancing provider education. However, the Atlanta study findings [15] suggest that unsupportive health insurance environments may be a major remaining impediment to scaling up the use of PrEP enough to radically decrease the incidence of new HIV infections across the United States. Availability of an evidence-based, effective HIV prevention intervention should not be dictated by geography, so advocacy to ensure equal access will be essential if the use of antiretroviral PrEP is to have a major impact on HIV incidence.

Notes

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