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EDITORIAL

Investing in People Who Inject Drugs: A PrEPonderance of Opportunities

In 2014, with more than 10 randomized efficacy trials on preexposure prophylaxis (PrEP), the Centers for Disease Control and Prevention (CDC) published clinical practice guidelines on the use of PrEP for high-risk individuals. Citing the Bangkok Tenofovir Study (1), which reported a 49% reduction in HIV incidence (PrEP efficacy) among people who inject drugs (PWID), the CDC recommended PrEP as "one prevention option for adult injection drug users at substantial risk of HIV acquisition" (2).

In *Annals,* a respected, widely published team of HIV-simulation modelers examines the following questions of PrEP for PWID: What is the public health benefit? Is it cost-effective? What budget would be required to finance a PrEP for PWID initiative? (3) Using a calibrated, compartmental, U.S.-based transmission model of HIV disease—complete with behavioral details related to age- and sexual-mixing, injection drug use and opioid substitution therapy, and HIV disease detection—these authors examined increasingly intensive strategies for delivering PrEP.

Bernard and colleagues' results bring to light several key points. First, implementation of a PrEP strategy is only clinically and economically efficient if accompanied by both HIV screening and early and immediate antiretroviral therapy (ART) for newly identified cases of infection. Second, at base-case estimates of PrEP uptake among PWID (25%), PrEP efficacy (49% incidence reduction), and annual costs ($10 000), the PrEP+Screen+ART package could prevent 21 500 new infections over 20 years, at an incremental cost-effectiveness ratio (ICER) that would exceed $250 000 per quality-adjusted life-year (QALY). This ICER falls substantially above the somewhat arbitrary but often used $100 000 or less per QALY standard for good economic value. Finally, the cost of providing PrEP to 25% of PWID, exclusive of costs for infrastructure development, would total about $2.2 billion annually ($44 billion over 20 years), nearly 10% of the 2015 federal HIV/AIDS budget.

Recognizing that the mainstay of PrEP, tenofovir, is anticipated to become generic in 2017 and that generic availability offers the potential for it to be combined more easily and less expensively with the already generic lamivudine, Bernard and colleagues examined the sensitivity of their results to changes in PrEP costs. Whereas a 65% reduction in PrEP costs would bring the ICER to less than $100 000 per QALY, providing PrEP to PWID would still cost $17 billion over 20 years.

Last year in Austin, Indiana, 181 new cases of HIV infection among PWID were epidemiologically linked within about 6 months (4). Although Bernard and colleagues show that PrEP for PWID is expensive, it is fair to ask whether a comprehensive PrEP policy might have prevented such an outbreak. Before the HIV outbreak in rural Austin, few PWID were insured or had regular access to medical care, few people had cars, and the closest HIV care provider was more than 30 miles away—all challenges that would hinder PrEP implementation. In addition to survey data indicating that fewer than half of PrEP prescribers are likely to offer it to PWID (5), these realities highlight the notable barriers to initiating a PrEP program for this group. To curtail the outbreak, active Austin PWID would have needed to effectively reach care; find a PrEP-informed, willing prescriber; and be able to afford, fill, and remain adherent to the PrEP prescription.

There is no question that the United States is immersed in a scourging opioid crisis. Deaths in 2014 associated with overdose eclipsed 47 000 (more than 28 500 of which were specifically associated with opiates), a statistic comparable to that of the peak U.S. HIV-related mortality rate in 1995 (n = 50 000) (6). Annual deaths from HIV have sharply declined while the rise in annual opioid deaths remains unabated. And, at an estimated $72 billion annually, the medical cost of treating patients with opioid abuse—who are increasingly prevalent on hospital floors—rivals that of HIV (7). Despite this surge in opioid use and PWID, HIV infection in this population has markedly declined: In 1991, 31% of HIV infections were among PWID; in 2014, that fraction dropped to about 6% (6).

With growing opioid analgesic use as a clear precursor to heroin injection and with the associated adverse outcomes of both, large national and state-based efforts have emerged in the fight (7). In 2014, the Drug Enforcement Agency increased restrictions on hydrocodone from schedule III to the more restrictive schedule II, eliminating the availability of refills. In January 2016, the New York State Department of Health partnered with CVS to make the opiate reversing agent naloxone available over-the-counter. In March 2016, the CDC published its first guidelines on opiate prescribing for chronic pain (8), President Obama pledged to increase federal government support for medication-assisted therapy, and Massachusetts passed a new law that limits the pill count in opioid prescriptions and provides substance abuse screening in public schools. The Comprehensive Addiction and Recovery Act of 2016, the goal of which is to convert addiction from a criminal activity to a public health challenge and to expand opiate replacement programs, is now winding its way through Congress with already overwhelming bipartisan support in the Senate. However, the Act will provide no more than the previously allocated $400 million over 5 years (about $80 million per year) for drug treatment—less than half the amount requested by the White House.

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As biomedical advances finally hold the promise of both effective HIV prevention and durable virologic suppression, it may seem heretical to disfavor investments in PrEP for PWID. But now is the time to be maximally efficient (dare we even say frugal?) with HIV prevention resources to ensure their greatest impact, because the problems related to PWID (such as the immediate and high mortality associated with overdose) are far greater than the no-longer-deadly threat of HIV itself. What good is preventing HIV if we do not first save that life at HIV risk? Investments in access to naloxone therapy (9), medical insurance and detoxification programs, opioid agonist therapy, and needle exchange will serve not only to prevent HIV infections (in some cases, at incident-reduction efficacies of 56% to 64%, higher than that of PrEP), they may simultaneously prove to be immediately life-saving (10).

Even if we agree that PrEP for PWID may one day be inexpensive enough to be demonstrably cost-effective as well as sufficiently accessible to prevent outbreaks like that in Indiana, Bernard and colleagues remind us of an important lesson, with PrEP for PWID as the case example. All that is cost-effective may not be affordable, and such resources might well be more efficiently leveraged.

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