

ENTRY POINT

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HIV Prevention Drug's Slow Uptake Undercuts Its Early Promise

Initially billed as a game changer, Truvada has faced multiple obstacles to widespread adoption.

BY DAVID TULLER

In 2010 a major study of men who have sex with men reported that a daily dose of an antiretroviral medication, Truvada, was extremely effective in preventing HIV infection.¹ Just before the results were publicly released, one of the study's many coauthors, a Boston physician named Kenneth Mayer, met with medical colleagues, health officials, and other local stakeholders to share and explain the new development. As he presented the findings, he recalls, his eyes welled up with tears.

"I felt very emotional," says Dr. Mayer, medical research director of Boston's Fenway Institute, which focuses on research on LGBT health and HIV treatment and prevention. "The intense emotions were the elation that after more than two decades of conducting HIV prevention research, we finally had a new powerful tool to prevent new infections, and sadness thinking of all the friends and patients I lost to AIDS, and the caprices of fate and time."

Yet eight years after those seminal results were reported, and six years after the Food and Drug Administration (FDA) formally approved the HIV treatment approach known as preexposure prophylaxis (PrEP), the uptake of this intervention has been slower than many researchers, clinicians, and public health officials had hoped. According to the most recent data, which include most prescriptions written in the US,

145,000 people have initiated the regimen.² That figure represents a fraction of the estimated 1.2 million at risk for HIV infection in the US that the Centers for Disease Control and Prevention believes could benefit from PrEP.³

The slow pace of adoption should not be considered surprising, says Jim Pickett, director of advocacy at the AIDS Foundation of Chicago. Pickett leads the Chicago PrEP Working Group, a coalition of more than 300 local stakeholders seeking to expand use of the intervention. Innovative strategies, he notes, frequently take time to attain optimal penetration. In this case, the new approach upended decades of practice in which, apart from abstinence, the consistent use of condoms was considered the most reliable prevention method.

"I think it really freaked people out," says Pickett. "It was paradigm shifting, it was revolutionary, and changing decades of dogma is hard." Those who thought it would be easy to implement, he adds, failed to consider the challenges involved. "Diffusion of innovation...is a slow process, and painfully slow in some cases," he says.

Obstacles To Uptake

The high retail cost of Truvada—more than \$1,000 a month—was an early barrier to widespread adoption of PrEP. But despite some initial hesitation, many private and public insurance plans now cover the drug. In particular, the

expansion of eligibility for Medicaid under the Affordable Care Act has helped many people access Truvada who would not otherwise have been able to, say proponents. Those gains could be at risk if the administration of President Donald Trump ends up reshaping the health care system by weakening the ACA or making significant cuts in Medicaid.

But public health officials, HIV advocates, and clinicians have cited multiple additional factors besides cost and insurance access that have limited the uptake of PrEP. These include concern among providers about prescribing a powerful medication to healthy people, controversy within the gay community about the wisdom of the approach, and lack of awareness of the drug among disadvantaged populations at greatest risk for HIV infection.

Reluctance on the part of providers has definitely played a role, says Mark Illeman, a physician assistant in San Francisco. While he has been enthusiastic about PrEP from the beginning, he noticed that many of his colleagues were not initially comfortable recommending the intervention, even though Truvada had been used for years to treat HIV infection before it was approved for preventive use. "There were lots of unanswered questions," he says. But over the past few years, he adds, attitudes have gradually changed—not only among patients but also among local clinicians. "It's caught on really well in San Francisco," he says.

In 2015, three years after the FDA approved this new indication for Truvada, a national survey of primary care providers revealed that two-thirds were aware of PrEP, but only 7 percent had prescribed it.⁴ "Although awareness and prescription are both on the rise, the former continues to be much more prevalent," noted a 2017 qualitative study of provider attitudes toward PrEP in *AIDS Patient Care and STDs*.^{5(p197)}

While Truvada offers almost complete protection from HIV infection when taken as prescribed, it is much less effective if people on the regimen skip too many doses. Within the gay community, many

men who came of age during the early years of the epidemic, including clinicians, have expressed concerns about the possible negative consequences for people who count on PrEP for protection but fail to take it consistently. If PrEP users are inconsistent in taking the daily dose and become infected without realizing it, the virus they carry could soon become resistant to the drug. It could then be transmitted to other HIV-negative sexual partners, even those who are on PrEP.

In 2015 the AIDS Healthcare Foundation (AHF), one of the largest providers of health care to people with HIV/AIDS, published an advertorial titled “The War against Prevention” in LGBT publications across the country. It cited statistics on nonadherence among PrEP users and criticized the use of HIV prevention funds to promote widespread access to PrEP. “In the debate surrounding PrEP, emotional appeals for sexual liberation have trumped medical science,” it declared.⁶ While acknowledging that PrEP could be appropriate for “specific patients,” the advertorial stated that “mass PrEP administration is a dangerous experiment.”

To date, the AHF’s worst fears do not appear to have been realized. So far there have been three well-documented cases of PrEP failure, with two of them attributable to Truvada resistance.^{7,8} Of course, similar cases could be occurring undetected. Others involved in HIV care have taken strong issue with the AHF’s opposition to the promotion of PrEP as a public health intervention.

Beyond inconsistent adherence, providers have also been concerned about possible side effects, since Truvada can impair patients’ renal function and reduce bone density. Another worry has been that PrEP users would engage in risk compensation—altering their sexual behavior because they believed they were no longer subject to HIV infection. “Some providers have expressed reluctance to offer PrEP for fear of patients decreasing their use of condoms, increasing their number of sexual partners, or otherwise adjusting their behavior in a way that enhances their sexual health risk in response to PrEP initiation,” noted the *AIDS Patient Care and STDs* study.^{5(p197)}

The authors, including Dr. Mayer,

acknowledged that some studies have documented reductions in condom use among PrEP users—a concern highlighted in the AHF’s advertorial. But the study noted that the available data suggest that “PrEP may more than offset increases in risk behavior.”^{5(p197)}

As an example, the authors cited research from a San Francisco clinical setting that found no new HIV infections among a sample of close to 700 PrEP users, even though many had acknowledged reduced reliance on condoms.^{5(p197)} They pointed out that people on statins also engage in risk compensation but do not face the same condemnation as those who might change their sexual behavior while on PrEP.

The role of condoms among PrEP users has been a controversial issue. PrEP was investigated and approved by the FDA as an addition to condom use, not as a replacement for it, and many health care providers have reinforced that message. But HIV advocates generally recognize and accept the fact that many men on PrEP who have sex with men do not always use condoms consistently, if at all. To encourage PrEP use, the PrEP4Love campaign, created by the Chicago PrEP Working Group, includes the following message: “You may be drawn to PrEP because of a desire for intimacy and connection you may not feel when wearing condoms. For the prevention of HIV, PrEP taken consistently and correctly is actually more effective than condom use.”⁹

Pickett says that those involved in HIV advocacy and education have generally recognized this reality. “If people used condoms consistently and correctly, we would not have a global fight to end HIV,” he says. “The fact is that PrEP was designed for people who don’t use condoms all the time.” Continuing to stigmatize those who choose not to use condoms can undermine prevention efforts, Pickett adds, but he believes that attitudes are changing. “We have come a long way from the kind of finger-pointing, shaming, and shouting that we had earlier,” he says.

At the same time, the Chicago PrEP Working Group’s PrEP4Love site acknowledges the role of condoms in preventing other sexually transmitted infections (STIs).⁹ To be sure, the advent of PrEP has been accompanied by a con-

current rise in diagnoses of gonorrhea, syphilis, and chlamydia, among others. However, proponents of the intervention note that this rise began years before PrEP became widely available.¹⁰

Damon Jacobs, a New York psychotherapist who hosts an online PrEP information and discussion page on Facebook, further notes that providers require PrEP users to undergo regular testing for HIV and STIs. Reported increases in STI diagnoses among those on PrEP might therefore be viewed as an artifact of increased engagement with the health care system, he points out. “There’s a myth that PrEP uptake causes higher rates of STIs, and the data do not support that,” he says. “PrEP allows people to be connected to health care, so they’re getting tested and treated now.”

Disparities In Uptake

Not surprisingly, the dissemination of PrEP among different socioeconomic groups has been uneven. Middle-class gay white men are disproportionately represented among the early adopters of PrEP—even though this demographic group is at less risk for HIV infection than African American and Latino men who have sex with men and transgender women and men. Although 44 percent of new HIV infections in 2015 were among African Americans, for example, they accounted for only an estimated 13 percent of PrEP users.¹¹ Latinos represented 24 percent of new infections but just 18 percent of PrEP users. Whites accounted for 62 percent of PrEP users but only 26 percent of new infections.

Disadvantaged population groups have higher infection rates not necessarily because their members engage in riskier behaviors but because they are more likely both to have untreated STIs that facilitate HIV transmission and to encounter others who are infected with HIV but are not on medications that suppress viral replication.¹² Research has consistently shown that people with undetectable viral loads cannot effectively transmit HIV to others.¹³

In Chicago, Esperanza Health Centers runs three community-based clinics and is making a concerted effort to increase PrEP uptake in the city’s Latino community, says Carmen Vergara, the organization’s chief operating officer. Many

Latinos, especially newer immigrants, are only vaguely aware of PrEP, so education is key. But even those who know about it and might want to try it face a major structural barrier: limited access to culturally sensitive and Spanish-speaking clinicians with whom patients feel comfortable discussing sexual matters. “There aren’t too many providers within the area who are prescribing PrEP, and we are trying to remove that barrier,” says Vergara.

According to Ricardo Cifuentes, Esperanza’s director of external affairs, another reason for the lag in uptake is that PrEP has often been promoted and marketed with sexualized images that may be less effective in communities with greater stigma related to sex. As a result, he says, many young Latino men who have sex with men appear to believe that PrEP is for “promiscuous” guys—an assumption that can reduce their interest in adopting the intervention.

“The very first thing when we considered any kind of marketing was not to exacerbate the problem by using language that might reinforce that barrier,” Cifuentes says. “If there’s someone in a state of undress, that might not be the kind of presentation that someone in the neighborhood would really respond

to. A message more about keeping yourself healthy and protecting yourself from HIV might get someone...to explore what PrEP is about.”

Beyond specific concerns about PrEP, Latinos and African Americans also often harbor a general mistrust of the medical and public health establishments because of a long history of discrimination and mistreatment, says John Schneider, a physician and researcher at the University of Chicago. To overcome such concerns, he and several colleagues are investigating whether social network interventions, such as educating key community members in how to talk to peers about PrEP, could increase uptake.

“At the center of this intervention is the premise that the social networks among young Black MSM [men who have sex with men] can be effective mechanisms of information diffusion, behavioral influence, social support, and personal and community empowerment and, therefore, are optimal leverage points for inducing adoption of an HIV prevention technology like PrEP,” they wrote in a recent article that described one such intervention in the journal *Clinical Trials*.¹⁴

In any event, the current one-a-day

Truvada regimen is considered just the beginning for the future of PrEP. Gilead is currently testing a variant of Truvada that is believed to have fewer side effects, and other antiretrovirals could also prove to have similar preventive properties. Researchers are investigating other approaches that could facilitate more widespread adoption, such as injectable formulations that could provide protection or regimens focused on taking the medication before and after a sexual encounter rather than daily.

As a case study of the diffusion of innovation, PrEP confirms what research has generally documented: The uneven penetration of new health care technologies tends to reflect existing societal patterns of socioeconomic status. Increased acceptance and use among disadvantaged groups will depend upon medical advances and policy developments that address the obstacles faced by people with less access to health insurance, reliable information, social capital, and other essential material and nonmaterial resources. ■

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NOTES

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