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Pre-exposure Prophylaxis in Primary Care—A New Era in HIV Prevention

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Pre-exposure prophylaxis (PrEP) is a powerful new prevention tool for those at substantial risk of acquiring HIV and can be used in combination with other HIV prevention methods. The antiretroviral single tablet combination containing emtricitabine and tenofovir (Truvada, Gilead Sciences Inc, Foster City, California) was approved by the Food and Drug Administration for this use in 2012 and formally recommended by the US Centers for Disease Control and Prevention (CDC) in May of 2014.¹ When taken as prescribed, PrEP provides 92% to 99% reduction in risk of acquiring HIV,² but it represents a significant paradigm shift in HIV prevention—the first time that a medication has been used to prevent HIV prior to exposure.

Because PrEP requires a prescription for Truvada, this new HIV prevention strategy lies squarely within the bounds of clinicians, and in most cases, beyond the scope of public health departments and community organizations that have traditionally worked to advance HIV prevention. While these groups can raise awareness and generate interest in the use of PrEP, its prescription will depend on clinicians.

Unfortunately, many clinicians are unfamiliar with PrEP and unaware of the recent CDC recommendation that all individuals at high risk of HIV should consider daily use of Truvada. To reach its full potential as an HIV prevention tool, clinicians must be aware of PrEP, be comfortable discussing it with patients, and either prescribe it or know where to refer interested patients. PrEP should be viewed as and offered like any other preventive health care service for high-risk patients.

Background

There are more than 8000 individuals estimated to be living with HIV in Wisconsin. On average, approximately 250 Wisconsin residents are diagnosed with HIV each year, a number that has remained steady for the last decade.³ At the same time, the prevalence of

HIV in African American men who have sex with men in Milwaukee is a staggering 32%, and the number of new diagnoses in young black men who have sex with men nearly tripled from 2004 to 2013. More than half of African American men who have sex with men newly diagnosed with HIV in 2014 were younger than 25 years old. HIV also continues to disproportionately affect gay and bisexual men of all races.

While it is estimated that conventional HIV prevention methods—such as behavioral risk reduction interventions, condom distribution, and HIV testing and counseling—have prevented millions of cases of HIV since the beginning of the epidemic, the unwavering rates of new infections both nationally and in Wisconsin suggest that additional strategies are needed. Recent research highlights the limitations of condom use as a primary HIV prevention strategy. CDC researchers retrospectively analyzed condom use and HIV infection from 2 different studies and found that among all men having anal sex, condoms were 70% effective for preventing HIV transmission with typical use.^{4,5} The researchers also found that condom use was difficult to maintain over the long term, with just 16% of participants reporting 100% condom use with any anal sex over the 3-year period.

Safety and Efficacy of PrEP

Several large, international, randomized controlled trials have demonstrated that PrEP resulted in significant reductions in HIV incidence among men who have sex with men,⁶ high-risk heterosexual adults;⁷ including HIV serodiscordant couples,⁸ and people who inject drugs.⁹ A key lesson learned from these trials—and several others that failed to demonstrate effectiveness—is that, as with any prevention method, PrEP is highly dependent on adherence in order to effectively lower the risk of HIV acquisition. Compared to other HIV prevention strategies, daily oral chemoprophylaxis has several unique advantages. Condoms and other barrier protection methods require both that users anticipate sexual activity by having condoms readily available and that they successfully and properly use them. Reliance on individuals' ability to carry out condom use during sexual encounters demonstrates one of the weaknesses of this prevention method, as individuals may be distracted from a disease prevention mindset due to the aroused state created by sexual engagement. In addition, many individuals engage in sexual encounters while under the influence of alcohol or drugs, further reducing the likelihood of successful condom use. By contrast, successful use of PrEP is accomplished by taking one pill on a routine basis, outside of the emotionally charged atmosphere of a sexual encounter.

Implementation of PrEP

For individuals to realize the potential benefits of PrEP, 3 elements are required: (1) awareness of PrEP by individuals at risk for HIV infection; (2) awareness of PrEP by clinicians; and (3) familiarity among clinicians with prescribing PrEP or knowledge of where to refer patients for PrEP. Health care professionals need to be part of each of these steps so that they can raise awareness in patients who they feel could benefit from PrEP, but may be unaware of it, or to respond to individuals who themselves are requesting PrEP and are looking for a prescriber.

During the past 3 years, we began implementing PrEP within our 2 academic Infectious Disease/HIV clinics. As the largest providers of HIV-related care in our regions, we have seen a steady increase of patients seeking PrEP, but have been disturbed by the difficulty that many patients have had in finding our respective clinics. Many patients describe asking their primary care clinicians about PrEP, only to have been met with reactions that include discouragement, indifference, or lack of awareness. When they have been successfully linked to a PrEP provider, it has much more often been a result of their own initiative and persistence, rather than at the recommendation of their clinician.

Our experience suggests that a combination of low awareness of PrEP among clinicians and at-risk individuals has resulted in extremely low uptake in Wisconsin. We estimate that only approximately 100 individuals are currently taking PrEP in Wisconsin,⁹ while estimates from other states in our region, Tennessee, and Ohio, range from 1000 to 2000 individuals.¹⁰ In Wisconsin as in the United States overall, men who have sex with men, particularly African American men, experience extremely disproportionate HIV incidence and prevalence.³ However, not every member of these demographic groups is at an elevated risk of HIV infection, and identifying those who could benefit most from PrEP requires knowledge of each patient's risk factors. Prior research indicates that most clinicians do not routinely ask about same-sex behaviors, and patients often do not disclose their sexual orientation without being asked.^{11–13} Thus, identifying individuals appropriate for PrEP requires discussion of sexual and other HIV risk factors. While having such conversations may represent a change in practice for some clinicians, the potential benefits of PrEP when targeted to patients at high risk for HIV are large. (See Table for summary guide for PrEP use combining our clinics' experience and CDC guidelines.)

Concerns

Concerns have been raised about the cost of Truvada, which is more than \$1300 per month.^{14–16} However, when used as PrEP, Truvada is not necessarily intended to be taken for a lifetime, as is the costlier combination antiretroviral treatment for established HIV infection. Modeling studies suggest that the costs associated with PrEP are in line with other common preventive health measures when delivered to appropriate populations, and the required lab monitoring is relatively inexpensive when compared to the monitoring required for those who are HIV positive and living near normal life expectancies on antiretrovirals.

In general, insurance programs cover the cost of Truvada as PrEP, and patient assistance programs are available for many individuals with high copays or who are underinsured. In our experience, however, many patients seeking PrEP were unaware that they were eligible for government-sponsored insurance or subsidies for commercial health insurance, and there remain individuals who are ineligible for or unable to obtain health insurance. Thus, further action, such as Medicaid expansion or development of other funding mechanisms, is needed to provide PrEP to those at highest risk.

Some public health experts have raised concerns that PrEP will encourage unsafe sexual practices, including less condom use and therefore higher rates of sexually transmitted infections (STI). However, in our experience, some individuals seeking PrEP already have very poor condom use, which in some cases has actually improved after initiating PrEP.

Other patients have consistent condom use, but are seeking additional protection. Further, the consequences of most STIs pale in comparison to HIV—both for individuals as well as the health care system—and once started on PrEP, patients are more engaged in the health care system, which creates opportunity for ongoing counseling regarding sexual health, STI screening, and HIV testing.

Sexually Transmitted Infections/Sexual Health

PrEP should be implemented as a comprehensive HIV prevention strategy and should be used as an opportunity to promote sexual health and wellness, including complete STI testing. Despite CDC recommendations that sexually active gay and bisexual men be screened annually at all sites at risk for infection, we found low implementation of this testing and high rates of infection among patients seeking PrEP, prior to being seen in our clinics. Most of these patients were not aware of recommendations for testing of extra-genital sites and had only had urethral screening in the past. This is especially concerning because STIs are a known risk factor for HIV acquisition.

Since implementing PrEP in our clinics, we have found an alarming number of extra-genital STIs (rectum and pharynx) at initial clinic visits, the majority of which were asymptomatic. Notably, we have found no urethral infections through nucleic acid amplification testing of urine specimens, which is the approach to screening most widely adopted in primary care settings.

Conclusion

The need for improved HIV prevention measures is clear. PrEP provides an additional, safe and effective measure for those at highest risk. Unlike other prevention measures, PrEP requires an encounter with a clinician, thereby providing an opportunity to optimize health for populations that may not otherwise see a need to access the health care system. Assessments for PrEP need to start in primary care and implementation should begin with support from infectious disease and HIV experts, with the eventual goal of implementation in primary care as clinician comfort grows, just like any other preventive health care service. PrEP provides a unique opportunity for health care professionals to make an impact on reducing the unacceptably high rate of new HIV diagnoses and the intolerable racial disparities that affect the people of Wisconsin.

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Summary of Guidance for Pre-exposure Prophylaxis (PrEP) Use

Table.

Men Who Have Sex With Men	Heterosexual Women and Men	People Who Inject Drugs
Detecting Substantial Risk of Acquiring HIV Infection		
Sexual partner with HIV Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work	Sexual partner with HIV Recent bacterial STI High number of sex partners History of inconsistent or no condom use Commercial sex work Lives in high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)
Clinically Eligible		
Documented negative HIV test before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function (serum creatinine), no contraindicated medications		
Prescription		
Daily, continuing, oral doses of TDF/FTC (Truvada), 90 day supply Follow-up visits at least every 3 months to provide: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months after, assess renal function Every 6 months test for bacterial STIs Document hepatitis B virus infection and vaccinate non-immune individuals		
Other Services		
Do oral/rectal STI testing	Assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

Abbreviation = sexually transmitted infections, STI.

Source: US Public Health Service.¹