PERSPECTIVE



Hidden in Plain Sight: Identifying Women Living in the United States Who Could Benefit From HIV Preexposure Prophylaxis

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HIV preexposure prophylaxis (PrEP) with oral tenofovir/emtricitabine is an effective means of decreasing human immunodeficiency virus (HIV) acquisition among women. However, few women are prescribed and are taking PrEP. This article offers perspectives on barriers to use and strategies to increase uptake among women. **Keywords.** pre-exposure prophylaxis; PrEP; HIV and women.

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Recent advances in antiretroviral therapy, increased virologic suppression, decreased transmission probability, and enhanced community awareness have contributed to a decline in the rate of new human immunodeficiency virus (HIV) infection among women living in the United States. The annual rate of HIV diagnoses among women decreased from 12.9 to 5.2 per 100 000 population between 2007 and 2017 [1, 2]. A total of 19% of all new HIV infections in the United States occur in women, down from approximately 27% in 2006 [3, 4]. Although this is a laudable achievement, these data belie the fact that many women remain at high risk of infection. Regional and racial differences in the HIV infection incidence have created hot spots of infection. Southern women have the highest rate of new diagnoses among women. Among black women, the rate of HIV infection diagnosis is 15 times and 5 times higher than among white women and Latino women, respectively [2,5].

Conversely, white women have been disproportionately impacted by recent injection drug-related HIV outbreaks (either by sharing needles or having sex with a male individual who injected drugs) [6]. Furthermore, women living in the United States are a diverse group that include non-US born or immigrant individuals. Surveillance data from the Centers for Disease Control and Prevention (CDC) demonstrate that new infections are disproportionately occurring among non-US-born women from sub-Saharan Africa, the Caribbean, and Latin America [7, 8]. These women may have acquired HIV overseas before migration or in the United States after migration, and they have largely been ignored by HIV prevention efforts.

Antiretroviral preexposure prophylaxis (PrEP) with daily oral coformulated tenofovir/emtricitabine is an effective means of decreasing HIV acquisition that could provide needed protection for many women living in the United States [9]. CDC guidelines suggest PrEP should be prescribed for women who are at "substantial risk" of HIV acquisition. A woman at "substantial risk" is defined as an HIV-negative woman who has had any sex with male partners in the past 6 months, who is not in a monogamous partnership with a recently tested HIV-negative partner, and who either (1) infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (ie, an injection drug using or bisexual male partner), (2) is in an ongoing sexual relationship with an HIV-positive partner, or (3) has had a bacterial sexually transmitted infection diagnosed or reported in the past 6 months [10]. Women who inject drugs and share equipment are also at "substantial risk" and should be offered PrEP. In addition, PrEP should be discussed with women in serodiscordant relationships during preconception and pregnancy as an additional tool to reduce the risk of sexual HIV acquisition [10]. According to the CDC, >170 000 women had indications for PrEP use in 2015. However, only 2.1% were prescribed PrEP [11, 12]. Inequitable prescription of PrEP may further promote racial and ethnic disparities; among women prescribed PrEP in 2016, nearly 6 times as many were white than black [12].

Numerous barriers to PrEP uptake among women have been identified. Few women are aware that PrEP exists [13]. In a recent analysis of nationally representative data, only 14.1% of high-risk women knew that there is a drug that could be prescribed to prevent HIV transmission [13]. Other studies have noted even lower levels of PrEP awareness among

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high-risk women [14]. Barriers related to cost, stigma regarding the use of "HIV medications", concerns regarding potential side effects and efficacy, medical mistrust, and challenges discussing sexual health issues with providers have been noted [15]. PrEP access has not been scaled up in many lower income communities, and lack of proximity is associated with lower willingness to use PrEP [16]. Primary healthcare providers may prefer not to prescribe PrEP and instead refer candidates to infectious disease specialists, which may further limit access [17].

Paramount among barriers to optimizing PrEP uptake among women living in the United States is the failure to identify those at highest risk of infection. For healthcare providers, determining HIV infection risk among women is challenging. The current CDC guidelines and recently published US Preventive Services Task Force recommendations assume that women are able to accurately estimate and convey their risk to their provider, which presumes knowledge of their sex partner's risk, including HIV status, HIV testing history, and other sexual and substance use behavior [10, 18, 19]. However, many women are unaware of their partner's risk behavior [20]. Providers must also consider the environment in which their patients select sex partners and determine whether their patients' sexual network is within a geographic hot spot and confers a high risk of HIV acquisition. Given the need to conduct a risk assessment, busy generalists may defer exploring a women's need for PrEP because they perceive incident HIV infection to be rare among women and, therefore, of less concern in comparison to other healthcare needs, particularly among black and Latino women, who are also disproportionately affected by numerous other chronic diseases. In the largest longitudinal study designed to understand behaviors associated with the risk of HIV infection among US women, the annual incidence of HIV infection among the >2000 enrolled women was 0.32% [21]. Enrollees reported a spectrum of individual and partner-level sexual and drug use risk behaviors. However, no specific individual-level sexual behavior among participants was predictive of an increased HIV infection risk (conceivably because there were so few incident HIV infections). In a second study focused on HIV infection risk among black women living in lower-income communities, socioeconomic factors (eg, homelessness and receipt of Medicaid), older age (>35 years old), and sex partner characteristics, rather than sexual behavior, were associated with HIV infection [22]. These findings highlight the lack of direct correlation between risk and individuallevel behavior and the importance of sex partner and community characteristics. For healthcare providers, women who are at substantial risk of HIV infection in the United States may be hidden in plain sight, and identification requires awareness of characteristics other than individual-level sexual behavior (eg, ecological and sociodemographic factors) that are associated with this risk.

From a patient's perspective, choosing to engage in preventive health behavior, such as using PrEP, is predicated upon heightened self-perceived risk. One of the most common reasons for the lack of willingness to take PrEP among at-risk women is low or no self-perceived risk of HIV infection [23]. Interventions to improve self-assessment of risk among women are not widely implemented. Even if self-perceived risk is congruent with actual risk and PrEP is initiated, ongoing adherence is necessary to ensure efficacy. High levels of adherence (86% of doses [6 of 7] per week) seem to be required to achieve levels sufficient to prevent HIV transmission in the cervicovaginal tissue [24]. There are no data demonstrating the efficacy of event-driven PrEP for protection among women (unlike among men who have sex with men) [25]. Without prompting by a provider or a personal sense of risk, it is difficult to anticipate that women will fill a PrEP prescription and adhere to a daily regimen on a consistent basis, despite the importance of adherence to ensure PrEP efficacy. In the absence of tools to enhance accurate awareness of the risk of HIV infection and strategies to support ongoing adherence to PrEP, the use and efficacy of PrEP might be compromised.

To increase PrEP use among women living in the United States, the narrative of HIV prevention must change. Clinical guidelines should incorporate moreinclusive recommendations for PrEP education and eligibility for women. If a woman is sexually active with a male partner, is negative for HIV, and does not use condoms consistently, PrEP should be discussed as a component of comprehensive sexual health care, irrespective of partner characteristics. For sexually active women who live in hot spots and engage in condomless sexual intercourse, PrEP should be highly recommended. In addition, providers should proactively screen the health records of female patients for recent sexually transmitted infections and nonoccupational use of postexposure prophylaxis. Increasing self-perception of risk among women may prove more challenging. Because the aggregate HIV infection incidence is low in the United States, a more nuanced, culturally tailored approach to enhance women's understanding of their risk is warranted. HIV prevention messages and public health awareness campaigns that challenge women's incongruent real and self-perceived HIV infection risk are needed, as well as enhanced community and provider education. Interventions that include the availability of PrEP at community and online pharmacies, the use of mobile health services, and community health workers who are trained to provide PrEP navigation services should be developed to complement awareness campaigns. Although the creation of a specific profile of women at risk should be avoided, the roles of geography, immigration, individual and community-level socioeconomic disadvantage, and racism and discrimination in potentiating the HIV epidemic among women in the United States must be acknowledged and addressed. Engagement of key community stakeholders (including faith leadership and advocates) is needed to promote an understanding of the ongoing HIV infection risk in communities of color. Failure to address these issues will lead to continued suboptimal PrEP uptake, exacerbate existing disparities, and impede efforts to end the HIV epidemic among women in the United States.

Notes

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References

- Centers for Disease Control and Prevention. HIV/AIDS surveillance report, 2007. Vol 19. Atlanta, GA: CDC, 2009. https://www.cdc.gov/ hiv/pdf/library/reports/surveillance/ cdc-hiv-surveillance-report-2007vol-19.pdf. Accessed 12 June 2019.
- 2. Centers for Disease Control and Prevention (CDC). HIV surveillance report, 2017. Vol 29. Atlanta, GA: CDC, **2018**. http://www.cdc.gov/ hiv/library/reports/hiv-surveillance. html. Accessed 12 June 2019.
- 3. Centers for Disease Control and Prevention. HIV among women. https://www.cdc.gov/hiv/group/ gender/women/index.html. Accessed 12 June 2019.
- 4. Centers for Disease Control and Prevention. Estimates of new HIV infections in the United States. https:// www.cdc.gov/nchhstp/newsroom/

docs/fact-sheet-on-hiv-estimates. pdf. Accessed 12 June 2019.

- Prejean J, Tang T, Hall HI. HIV diagnoses and prevalence in the southern region of the United States, 2007– 2010. J Community Health 2013; 38:414–26.
- Peters PJ, Pontones P, Hoover KW, et al.; Indiana HIV Outbreak Investigation Team. HIV infection linked to injection use of oxymorphone in Indiana, 2014–2015. N Engl J Med 2016; 375:229–39.
- Demeke HB, Johnson AS, Wu B, Moonesinghe R, Dean HD. Unequal declines in absolute and relative disparities in HIV diagnoses among Black women, United States, 2008 to 2016. Am J Public Health 2018; 108:S299–303.
- Prosser AT, Tang T, Hall HI. HIV in persons born outside the United States, 2007–2010. JAMA 2012; 308:601–7.
- Baeten JM, Donnell D, Ndase P, et al.; Partners PrEP Study Team. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012; 367:399–410.
- 10. Centers for Disease Control and Prevention, US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. **2018**. https://www.cdc.gov/hiv/pdf/risk/ prep/cdc-hiv-prep-guidelines-2017. pdf. Accessed 12 June 2019.
- Smith DK, Van Handel M, Grey J. Estimates of adults with indications for HIV pre-exposure prophylaxis by jurisdiction, transmission risk group, and race/ethnicity, United States, 2015. Ann Epidemiol **2018**; doi: 10.1016/j.annepidem.2018.05.003.
- Huang YA, Zhu W, Smith DK, Harris N, Hoover KW. HIV preexposure prophylaxis, by race and ethnicity - United States, 2014–2016. MMWR Morb Mortal Wkly Rep 2018; 67:1147–50.

- Ojikutu BO, Bogart LM, Higgins-Biddle M, et al. Facilitators and barriers to pre-exposure prophylaxis (PrEP) use among black individuals in the United States: results from the National Survey on HIV in the Black Community (NSHBC). AIDS Behav 2018; 22:3576–87.
- 14. Patel AS, Goparaju L, Sales JM, et al. Brief report: PrEP eligibility among at-risk women in the Southern United States: associated factors, awareness, and acceptability. J Acquir Immune Defic Syndr **2019**; 80:527–32.
- Goparaju L, Praschan NC, Warren-Jeanpiere L, Experton LS, Young MA, Kassaye S. Stigma, partners, providers and costs: potential barriers to PrEP uptake among US women. J AIDS Clin Res 2017;8, pii: 730. doi:10.4172/2155-6113.1000730.
- 16. Ojikutu BO, Bogart LM, Mayer KH, Stopka TJ, Sullivan PS, Ransome Y. Spatial access and willingness to use pre-exposure prophylaxis among Black/African American individuals in the United States: cross-sectional survey. JMIR Public Health Surveill 2019; 5:e12405.
- 17. Krakower D, Ware N, Mitty JA, Maloney K, Mayer KH. HIV providers' perceived barriers and facilitators to implementing pre-exposure prophylaxis in care settings: a qualitative study. AIDS Behav **2014**; 18:1712–21.
- 18. United States Preventive Services Task Force (USPSTF). Preexposure prophylaxis for the prevention of HIV infection: US Preventive Services Task Force recommendation statement. JAMA **2019.** doi: 10.1001/ jama.2019.6390.
- Calabrese SK, Willie TC, Galvao RW, et al. Current US guidelines for prescribing HIV pre-exposure prophylaxis (PrEP) disqualify many women who are at risk and motivated to use PrEP. J Acquir Immune Defic Syndr 2019; 81:395–405.
- 20. Jennings L, Rompalo AM, Wang J, et al.; HIV Prevention Trials

Network (HPTN 064) Women's HIV SeroIncidence Study (ISIS). Prevalence and correlates of knowledge of male partner HIV testing and serostatus among African-American women living in high poverty, high HIV prevalence communities (HPTN 064). AIDS Behav **2015**; 19:291–301.

21. Hodder SL, Justman J, Hughes JP, et al.; HIV Prevention Trials Network 064; Women's HIV SeroIncidence Study Team. HIV acquisition among women from selected areas of the United States: a cohort study. Ann Intern Med **2013**; 158:10–8.

- Ivy W 3rd, Miles I, Le B, Paz-Bailey G. Correlates of HIV infection among African American women from 20 cities in the United States. AIDS Behav 2014; 18(Suppl 3):266–75.
- 23. Carley T, Siewert E, Naresh A. Interest in pre-exposure prophylaxis (PrEP) for HIV is limited among women in a general obstetrics & gynecology setting. AIDS Behav **2019**. doi: 10.1007/ s10461-019-02529-1.
- 24. Cottrell ML, Yang KH, Prince HM, et al. A translational pharmacology approach to predicting outcomes of preexposure prophylaxis against HIV in men and women using tenofovir disoproxil fumarate with or without emtricitabine. J Infect Dis **2016**; 214:55–64.
- 25. Molina JM, Capitant C, Spire B, et al.; ANRS IPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med **2015**; 373:2237–46.