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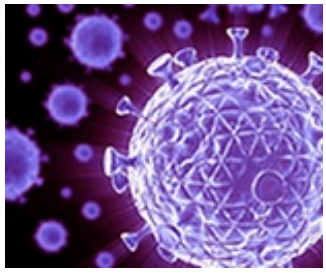

Addressing Barriers to Provider and Patient Engagement in PrEP

In this Issue...

Randomized studies have demonstrated that HIV pre-exposure prophylaxis (PrEP) is highly efficacious at preventing HIV acquisition. To date, however, uptake of PrEP has been limited in the United States. One of the major barriers to implementing PrEP is limited awareness of PrEP among health care providers. An additional barrier to scaling up PrEP is lack of awareness of PrEP among populations that experience high rates of new HIV infections.

In this issue, Dr. Douglas Krakower from Harvard Medical School reviews recent studies that have assessed awareness of and experience with PrEP among primary care providers, differential willingness of clinicians to prescribe PrEP to individuals with particular risk factors for HIV acquisition, provider biases in hypothetical prescribing decisions about PrEP, and limited awareness and use of PrEP among diverse populations at high risk for HIV infection.

LEARNING OBJECTIVES

- Discuss provider-related barriers to effective implementation of HIV pre-exposure prophylaxis (PrEP).
- Describe patient-related barriers to increased uptake of PrEP.
- Summarize potential disparities in awareness and access to PrEP among priority populations with high rates of new HIV infections.

GUEST AUTHOR OF THE MONTH

Commentary & Reviews

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Guest Faculty Disclosure

Dr. Krakower has disclosed that he has performed contract research for Gilead Sciences, Inc.

Unlabeled/Unapproved uses

Dr. Krakower has indicated that there will be references to the intermittent use of tenofovir-emtricitabine for use as PrEP.

IN THIS ISSUE

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Issue 3

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COMMENTARY

As there are 40,000 new HIV infections in the United States annually, there is a need to optimize implementation of effective HIV prevention strategies.[1] Randomized studies have demonstrated that HIV pre-exposure prophylaxis (PrEP), in which persons at substantial risk for HIV infection can use antiretroviral medications to protect against viral acquisition, is highly efficacious at decreasing HIV transmission. These studies have demonstrated the protective benefits of PrEP for multiple priority populations with high rates of new HIV infections, including men who have sex with men and transgender women, heterosexual men and women with HIV-infected sexual partners, and persons who inject drugs (PWID).[2-5] Additional observational studies have demonstrated that PrEP is feasible, acceptable, and likely to be effective at decreasing HIV transmission when prescribed to motivated, adherent patients during demonstration projects or as part of routine clinical care.[6,7]

Because of the preponderance of data suggesting that PrEP is safe and effective, the US Centers for Disease Control and Prevention (CDC) has issued formal guidelines recommending that clinicians consider PrEP as a prevention option for MSM, PWID, and heterosexuals who engage in high-risk behaviors.[8] CDC estimates that approximately 1.2 million Americans are likely to benefit from using PrEP, including one in four MSM (492,000), one in five PWID (115,000), and one in 200 heterosexuals (624,000).[9] To date, however, uptake of PrEP has been limited, with only about 100,000 individuals having been prescribed PrEP.[10] Without a deeper understanding of the barriers to effective uptake of PrEP, the public health benefits of PrEP are likely to remain unrealized.

Studies suggest that several clinician-related barriers have contributed to the slow uptake of PrEP, including limited awareness, knowledge, and experience with PrEP. In a national survey of primary care providers with diverse training backgrounds, Smith and colleagues (reviewed in this issue) found that (as of 2015) only 66% of respondents had heard of PrEP, only 7% of providers had prescribed PrEP, and overall knowledge of PrEP was limited. However, most of these providers would be willing to prescribe PrEP to patients from at least one priority population, and many providers expressed an interest in additional training about PrEP, suggesting that these practitioners might be receptive to educational and training interventions tailored to their needs.

Studies suggest that another provider-related barrier to effective and equitable implementation of PrEP is that providers may have differential prescribing patterns based on a patient's risk behaviors. Edelman and colleagues (reviewed in this issue) surveyed primary care providers and found that they would be less willing to prescribe PrEP to PWID than to MSM and heterosexual people with HIV-infected partners. Calabrese and colleagues (also reviewed herein) found that medical students, when presented with a vignette of a hypothetical MSM patient seeking PrEP, were more likely to anticipate risk compensation (ie, increases in sexual risk behaviors) and less willing to prescribe PrEP when presented with black patients than with white patients. This study suggests that health care professionals may be prone to implicit bias when approaching clinical decisions about prescribing PrEP to their patients, including race-related biases that can propagate racial disparities in providing access to PrEP. Together, these studies suggest that providers need educational interventions that specifically identify and address biases in their decision-making processes about the specific risk behaviors and racial characteristics of patients in their care.

In addition to these provider-related barriers, studies suggest that a major patient-related

barrier to PrEP use is lack of awareness of PrEP among individuals from priority populations. Khanna and colleagues (reviewed in this issue) found that only 40% of young black MSM were aware of PrEP, and only 3% of these men had used PrEP. Black MSM are one of the only populations in the US without substantial decreases in rates of new HIV infections in recent years.[1] These findings suggest an urgent need to develop interventions to disseminate knowledge and increase access to PrEP among young black MSM, which may be particularly challenging given structural barriers to accessing health care for these youths (eg, lack of insurance, poverty, limited health literacy)[11] and medical mistrust among racial and ethnic minority communities.[12] An additional (reviewed) study by Walters and colleagues found that PWID and heterosexual people from areas with a high prevalence of poverty and/or HIV infection in the New York City area were less likely than MSM to be aware of PrEP. In this study, awareness of PrEP was low in general, which suggests a need to deploy informational campaigns about PrEP to multiple priority populations, as well as to the health care providers and community-based organizations that serve these populations, to optimize PrEP uptake and to mitigate disparities in PrEP use.

In summary, limited awareness and experience with PrEP among both health care providers and individuals with risk factors for HIV acquisition represent important barriers to maximizing the impact of PrEP in the US. Moreover, disparities in provider willingness — whether conscious or subconscious — to prescribe PrEP to individuals with particular risk factors for HIV infection or racial identities, and differences in awareness of PrEP among specific priority populations, must be addressed to ensure that this highly efficacious intervention is implemented effectively and equitably.

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Priority Populations: Differential Awareness of Medications to Prevent HIV

Walters SM, Rivera AV, Starbuck L, et al. Differences in awareness of pre-exposure prophylaxis and post-exposure prophylaxis among groups at-risk for HIV in New York State: New York City and Long Island, NY, 2011-2013. *J Acquir Immune Defic Syndr.* 2017 Jul 1;75 Suppl 3:S383-S391.

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Of the 40,000 new HIV infections in the United States annually, 70% are attributable to male-to-male sexual contact, 23% to heterosexual sex, and 7% to injection drug use.[1] Guidelines from the US Centers for Disease Control and Prevention (CDC) recommend that PrEP and post-exposure prophylaxis (PEP) be considered as prevention options for men who have sex with men (MSM), persons who inject drugs (PWID), and heterosexual people who engage in high-risk sexual behaviors.[2,3] In this study, Walters and colleagues compared levels of awareness of PrEP and PEP among these three priority populations in New York City and Long Island, New York, which represent a region with a dense, urban HIV epidemic.

This study used data from the National HIV Behavioral Surveillance system collected in New York City and Long Island during 2011 to 2013 to measure awareness among different populations stratified by HIV risk group and other sociodemographic characteristics. The National HIV Behavioral Surveillance system includes anonymous, cross-sectional surveys that rotate annually among MSM, PWID, and heterosexual people living in high-prevalence areas for poverty and HIV. The primary outcome question for the current study asked participants if they had ever heard of people who do not have HIV taking anti-HIV medicines to protect themselves from becoming infected. Because this question could not be used to differentiate between awareness of PrEP versus PEP, the authors considered affirmative responses to represent awareness of “PrEP/PEP.”

Of 1455 respondents from New York City, 486 were MSM, 468 were PWID (122 [26%] female), and 501 were heterosexual (207 [41%] female); for Long Island, of 1028 respondents, 307 were MSM, 196 were PWID (32% female), and 525 were heterosexual (48% female). Samples were racially and ethnically diverse, although the PWID and heterosexual samples were predominantly black or Latino/a (Spanish culture or origin, regardless of race). MSM in both areas tended to be more educated and have higher incomes than PWID or heterosexual people.

Overall, awareness of PrEP/PEP was low, with 21% and 10% of participants indicating awareness in New York City and Long Island, respectively. For Long Island, in multivariable logistic regression models, all groups had significantly decreased odds of PrEP/PEP awareness compared with MSM (female PWID, $P < .01$; male PWID, $P < .001$; heterosexual females, $P < .01$; heterosexual males, $P < .01$). Similar trends were observed in New York City, though decreased odds of PrEP/PEP awareness was only significant for male PWID ($P < .01$).

The authors concluded that awareness of chemoprophylaxis might have spread through community-based networks and these networks could potentially be accessed to disseminate information about PrEP and PEP to individuals who could benefit from using these interventions. Future studies to identify the most effective ways to disseminate information about PrEP and PEP in diverse networks could help increase overall uptake of PrEP and PEP, as well address disparities in access to these protective strategies.

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Infection in the United States - 2014. A Clinical Practice Guideline. Available at: https://www.cdc.gov/hiv/pdf/prepprovidersupplement2014.pdf
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Priority Populations: PrEP Uptake

Khanna AS, Michaels S, Skaathun B, et al. Pre-exposure prophylaxis (PrEP) awareness and use in a population-based sample of young black men who have sex with men. *JAMA Intern Med.* 2016;176(1):136-138.

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Over the past decade, rates of new HIV infections have decreased modestly from 50,000 new infections annually to about 40,000 new infections each year. However, young black men who have sex with men (BMSM) represent one of the few populations in which rates of new HIV infections have not declined appreciably,[1] suggesting an urgent need to optimize PrEP and other preventive strategies for this critical population. In their study, Khanna and colleagues surveyed young BMSM in the South Side of Chicago, an area in which BMSM experience high rates of HIV infections, to assess awareness and experience with PrEP for this population.

The authors used respondent-driven sampling, an approach in which survey respondents are asked to recruit their peers for participation in the study, to enroll 622 young BMSM for survey completion during 2013 to 2014. Eligibility criteria included age between 16 and 29 years, being born male, identifying as African American or black, and having oral or anal sex with a male within the prior 24 months. In the final study sample, 39% of participants had high school/GED as their terminal education, 79% earned less than $20,000 per year, and 72% of the sample was HIV-noninfected and thus potentially eligible for PrEP. About half (48%) of the PrEP-eligible respondents had some form of health insurance coverage.

Only 40% of young BMSM had heard of PrEP, a proportion that did not change appreciably over the period of study enrollment. Twelve percent knew others who had used PrEP. Of the HIV-noninfected participants, 3.6% had experience using PrEP. Factors associated with being aware of PrEP included having a primary care provider, participating in an HIV prevention program or research study, having had rectal testing for sexually transmitted infections, and being a member of the House/Ball community (a network of social groups for sexual and gender minorities). Other risk factors for HIV acquisition, such as syphilis seropositivity, having group sex, and having sex while using recreational substances, were not associated with awareness of PrEP.

Clinic-based HIV prevention interventions for young BMSM were virtually nonexistent prior to the availability of PrEP.[2] The current study demonstrates that there is an ongoing need to invest in programs to raise awareness and facilitate more timely and widespread access to PrEP for young BMSM. This population faces multiple structural and psychosocial barriers to accessing PrEP, including low rates of insurance coverage, poverty, and intersecting forms of health care-related stigma (ie, homophobia and racism),[3] which likely contribute to the low rates of awareness and uptake of PrEP for young BMSM. The finding that individuals who had a primary care provider were more likely to be aware of PrEP suggests that interventions to engage front line clinicians in routine HIV risk assessments and discussions about PrEP for their young BMSM patients could improve access to this intervention. However, it is clear that multifactorial support for these youths, including support to overcome financial and insurance barriers to accessing PrEP, will be needed to realize the potential benefits of PrEP for this community.

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Awareness and Attitudes Toward PrEP Among US PCPs

Smith DK, Mendoza MCB, Stryker JE, Rose CE (2016) PrEP Awareness and attitudes in a national survey of primary care clinicians in the United States, 2009–2015. *PLoS One*. 2016 Jun 3;11(6):e0156592

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Smith and colleagues conducted repeated cross-sectional surveys of primary care clinicians in the United States to assess their awareness and attitudes toward HIV preexposure prophylaxis (PrEP). Surveys of around 1500 practicing physicians and nurse practitioners were conducted annually during 2009 to 2015 (except 2011), and 251 pharmacists were also surveyed in 2012. The study design provided an opportunity to track changes in awareness and attitudes toward PrEP before and after the release of important efficacy trials for PrEP published between 2010 and 2013.[1-4] Prior to 2010, attitudes toward PrEP were assessed based on a hypothetical efficacy estimate of 75%. After 2010, PrEP efficacy was presented as 90% or more among individuals using PrEP daily, and substantially less (< 50%) for those with lower adherence.

Survey invitations were sent to samples of health care professionals from several national databases, including members of Epocrates, SERMO (a social network for physicians), and others. Respondents most frequently identified as family practitioners/general practitioners (36%), internists (31%), nurse practitioners (17%) and obstetrician/gynecologists (17%); all four major geographical regions of the country (West, Midwest, South, and Northeast) were represented. About one-quarter of the respondents had experience prescribing antiretroviral medications for HIV treatment, and one-quarter also had experience prescribing these medications for occupational postexposure prophylaxis.

Only 24% of providers were aware of PrEP in 2009, but 66% were aware of PrEP in 2015 ($P < .001$). On a five-question, true-false knowledge assessment about PrEP presented in three survey years, the most common response was “don’t know” to four questions. Across most of the survey years, the majority of respondents supported PrEP use for one or more risk populations presented (91%). However, more clinicians were willing to provide PrEP to members of HIV serodiscordant couples (79%) than to men who have sex with men (MSM; 66%), persons who inject drugs (PWID; 63%), members of HIV serodiscordant couples planning to conceive (61%), persons who change sexual partners frequently (56%), and those with sexually transmitted infections (34%). Willingness to prescribe for at least one high-risk group or for discordant couples trying to conceive increased over time ($P < .001$).

Experience with PrEP was limited across all years but increased over time, with only 1% of clinicians reporting any experience with prescribing PrEP on surveys before 2013, 4% on 2013 and 2014 surveys, and 7% in 2015. In 2015, clinicians who had prescribed PrEP had done so for MSM (73%), PWID (22%), and heterosexual HIV serodiscordant couples (most often to women; 45%). Half of respondents (52%) cited formal guidelines from the US Centers for Disease Control and Prevention as having the greatest influence on their prescribing of PrEP, and most (83%) expressed interest in continuing medical education trainings about PrEP.

The findings of this study highlight that PrEP awareness has increased over time, but a minority of primary care providers might still be unaware of PrEP. Most primary care providers would be willing to prescribe PrEP to at least one priority population, and most

expressed an interest in additional training in PrEP, suggesting that this population of providers may be receptive to adopting PrEP into their practices. However, the authors' findings that clinicians were more willing to prescribe PrEP to individuals with particular risk factors for HIV acquisition than others (eg, heterosexual couples > MSM > PWID) suggests that provider biases could potentially result in disparities in access to PrEP. Overall, this study suggests that additional efforts to educate and train primary care providers in PrEP, with particular attention to addressing potential preconceived notions or misconceptions about the benefits of PrEP for certain priority populations, could increase engagement in PrEP for this important population of providers.

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PCPs' Willingness to Prescribe PrEP to PWID

Edelman E, Moore B, Calabrese S, et al. Primary care physicians' willingness to prescribe HIV pre-exposure prophylaxis for people who inject drugs. *AIDS Behav*. 2017 Apr;21(4):1025-1033

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In the United States, 7% of all new HIV infections each year are attributed to injection drug use.[1] Guidelines from the US Centers for Disease Control and Prevention (CDC) regarding HIV preexposure prophylaxis (PrEP) recommend PrEP as a prevention option for persons who inject drugs (PWID).[2] This recommendation is based on data from a randomized study of PWID in Thailand that demonstrated a 49% reduction in HIV incidence among PWID assigned to use PrEP compared to those on placebo.[3] In their study, Edelman and colleagues surveyed a convenience sample of 250 academic primary care providers who were members of the Society of General Internal Medicine to assess their willingness to prescribe PrEP to PWID in 2015.

The primary measure of willingness to prescribe PrEP was assessed using eight brief, hypothetical patient scenarios. Each of these scenarios represented patients with a different category of risk behavior considered to be an indication for PrEP according to CDC guidelines, including PWID, heterosexual men and women in HIV-serodiscordant partnerships or in relationships with individuals at risk for HIV infection, and men who have sex with men. Willingness to prescribe PrEP to each of these patients was measured using four-point Likert scales that were dichotomized as low (1 or 2) vs high (3 or 4) for analyses.

Nearly half (49%) of the respondents practiced in the Northeastern US, with most (85%) located at urban clinics at academic medical centers (68%), and most (86%) providing care to 20 or fewer HIV-infected patients. Compared to all other groups, willingness to prescribe PrEP to was lowest for PWID ($P < .001$). Providers indicated the lowest willingness to prescribe PrEP to PWID recently engaged in methadone treatment programs ($P < .001$), even though CDC guidelines specifically recommend that PrEP be considered for PWID with recent engagement in substance abuse treatment programs.[2] Across all scenarios, providers were most willing to prescribe PrEP to males or females in HIV-serodiscordant

couples. The only provider characteristic associated with willingness to prescribe PrEP to PWID was volume of HIV-infected patients in their care, with those providers delivering care to 20 or fewer HIV-infected patients indicating lower willingness to prescribe PrEP to PWID ($P < .01$).

The results of this survey suggest that academic primary care providers may be less willing to prescribe PrEP to PWID than to individuals with other risk factors for HIV acquisition in their practices. These findings are consistent with the national study of primary care providers by Smith and others[4] (reviewed in this issue); an additional national study of infectious diseases physicians, in which fewer than half of these specialists believed that PrEP should be routinely offered to PWID,[5] and with other studies of HIV specialists in several regions of the US.[6,7]

Fear of stigmatization is frequently reported by PWID as a barrier to accessing health care.[8] The results of these studies demonstrate that provider bias may prevent access to HIV preventive strategies such as PrEP. Recent HIV outbreaks among PWID, like one recently reported in Indiana,[9] demonstrate the importance of harm reduction strategies in this population. There is a need for comprehensive training interventions that can increase providers' willingness and confidence to prescribe PrEP to PWID and decrease their perceived stigma about this vulnerable population.

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Clinical Decisions About PrEP Prescribing: A Potential Source of Emerging Disparities

Calabrese S, Earnshaw V, Underhill K, Hansen N, Dovidio J. The impact of patient race on clinical decisions related to prescribing HIV pre-exposure prophylaxis (PrEP): Assumptions about sexual risk compensation and implications for access. *AIDS Behav.* 2014;18(2): 226-240.

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In the United States, African American communities experience disproportionately high rates of new HIV infections, with young, black men who have sex with men (MSM) experiencing some of the greatest disparities in HIV incidence among all priority populations.[1] Calabrese and colleagues explored medical students' willingness to prescribe PrEP to black vs white MSM seeking PrEP in hypothetical patient scenarios, to assess whether these students could be subject to implicit racial bias in their prescribing decisions (which has previously been documented for prescribing decisions related to HIV treatment).[2-4] These authors also explored whether racial stereotypes about sexual risk compensation (ie, increased sexual risk-taking while using PrEP) could mediate any race-related differences in prescribing decisions.

For this study, online surveys were administered to medical students attending medical schools in the northeastern US. Surveys included a patient vignette of a 31-year-old MSM patient seeking PrEP from his primary care physician in the context of having condomless sex with a monogamous, HIV-infected male partner. The only aspect of the vignette that was varied was patient race, with half of the students randomly assigned to review a vignette with a black patient and the remaining students assigned to review a vignette with a white patient. After reading the vignette, the students were asked to rate seven statements on a scale of 1 not likely to 5 extremely likely. Examples of the statements were "Predicted patient sexual risk compensation," "Predicted patient adherence," "Willingness to prescribe PrEP," and "General feelings toward the patient."

Of 102 students completing the survey, 48% were white, 41% were Asian, and 3% were black or African American; all stages of medical school training were represented (ie, first to fourth year in addition to "other" year). A significant between-group difference was found in predicted risk compensation, with participants in the black patient condition rating the hypothetical patient more likely to engage in increased sexual risk taking if prescribed PrEP than did participants in the white-patient condition (on the 5-point rating scale, 3.3 vs 2.9; $P < .05$). Moreover, the prediction of risk compensation was associated with decreased willingness to prescribe PrEP. Most students (87%) endorsed equally positive feelings toward black vs white patients.

The study findings suggest that race-related implicit (ie, subconscious) biases could affect prescribing decisions about PrEP, which has important implications for equitable access to PrEP among patients from different racial backgrounds. Early assessments suggest that PrEP uptake may be disproportionately low in black populations compared to white populations,[5] despite the relatively higher rates of HIV transmission in black communities, indicating a need for effective ways to counteract biases in prescribing decisions. A limitation of this study is that the participants were medical students instead of practicing clinicians. Nonetheless, the findings from this survey suggest that additional studies are needed to identify any race-related or other biases that might be present in the prescribing decisions of frontline clinicians, which can inform efforts to mitigate disparities in PrEP provision.

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KEY TAKEAWAYS

- HIV pre-exposure prophylaxis is highly efficacious at preventing HIV acquisition among persons at substantial risk for HIV infection; to date, however, uptake of PrEP has been limited in the United States.
- Lack of awareness and experience with PrEP among health care providers, as well as the potential for bias in health care providers' prescribing decisions for PrEP, represent impediments to optimal implementation of PrEP.
- Low awareness and use of PrEP among priority populations (eg, men who have sex with men, persons who inject drugs, and heterosexual people at high risk for HIV infection), as well as differential awareness of PrEP among these populations, represent additional barriers to effective and equitable implementation of PrEP.

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