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Time to make the jump: Translating HIV pre-exposure prophylaxis research into real-world public health impact

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To the Editors

We applaud the analyses elucidating the differences in HIV pre-exposure prophylaxis (PrEP) access in states with different public insurance programs (see Doblecki-Lewis S, et al.'s "Healthcare Access and PrEP Continuation in San Francisco and Miami").¹ Their open-label demonstration study evaluated 173 patients in San Francisco and Miami following completion of a National Institutes of Health sponsored PrEP demonstration project.² PrEP was originally provided free of charge at these sites during a three-year study. However, while 92% (159/173) reported interest in continuing PrEP after the study's conclusion, only 40% (69/171) of participants reported continuing PrEP four to six months after the study ended. Moreover, among individuals who did continue PrEP, 33% (23/69) reported a gap in taking medication; the average gap was close to two months. These important findings highlight the challenges associated with transitioning participants in research studies and demonstration projects to real-world clinical care programs; these challenges are particularly acute for men who have sex with men (MSM) of color who bear a disproportionate share of the HIV disease burden in the United States.

There are several reasons why patients may be better retained in PrEP care in research studies and demonstration projects than in real-world clinical settings. First, research

patients are often not charged for their visits or for PrEP medications, which can be cost-prohibitive for some patients, particularly those without or with limited insurance coverage. Patients may also forego high deductibles or co-payments that many insurance companies require for PrEP medications, laboratory work, and related clinical services.

Second, many research studies have staff resources to promote retention in care, which usually includes consistent outreach, regularly scheduled patient visits and reminders, transportation support, and other important case management services. Furthermore, research participants are usually financially compensated for attending visits, which bolsters retention in PrEP care. In contrast, in many non-research settings, support staff to promote retention in care is limited, patients are not compensated for attending routine clinical visits, and patients with limited insurance coverage often forego important PrEP services and medications. These phenomena may explain why rates of retention in PrEP care dropped precipitously when the San Francisco and Miami demonstration projects concluded.

Our own work highlights challenges with retaining patients in PrEP clinic care. In a three site study in real-world clinical settings, 57% (98/171) of patients were retained in PrEP care at six months.³ These findings were consistent across three diverse clinical settings in Jackson, Mississippi (61%; 37/61); Providence, Rhode Island (53%; 42/80); and Saint Louis, Missouri (63%; 19/30, $p=0.51$). However, our higher rates of retention in care reflect our efforts to integrate PrEP into clinical infrastructure rather than stand-alone research studies or demonstration projects. It is worth noting, however, that retention in care was also sub-optimal across all three of our clinical sites.

In randomized-controlled PrEP efficacy trials, many participants reported taking PrEP, but had low levels of the medication in their blood.^{4,5} Discordance between self-reported adherence and tenofovir blood levels may be because patients received other clinical care and financial compensation for study participation, and therefore continued to come to study visits even after discontinuing PrEP or having suboptimal adherence rates. This discordance was noted in the Vaginal and Oral Intervention to Control the Epidemic (VOICE) PrEP trial.⁶ Furthermore, in randomized control trials in which the product's efficacy had not yet been determined, patients' perceptions about taking placebos may also undermine adherence.⁷

Our own PrEP programs demonstrated that patients retained in care were overwhelmingly adherent to PrEP and that their self-reported adherence was confirmed with dried blood spots (L.M., unpublished data, 2016; R.R.P., unpublished data, 2016).⁸ Furthermore, patients who remained in PrEP care had initially reported risk behaviors or being members of sexual networks that might place them at high risk for HIV acquisition; 89% of our patients were MSM and 69% reported condomless anal sex at least once in the last three months.³ However, less is understood about the risk behaviors of patients who are *not* retained in care; it is conceivable that some individuals who are not retained may no longer need PrEP, and therefore discontinue PrEP care. On the other hand, it is conceivable that patients lost to follow-up are the most vulnerable and are at highest risk for HIV acquisition. These phenomena warrant further investigation in real-world settings.⁹

The Doblecki-Lewis study illustrates challenges with retaining MSM of color in PrEP care. Most MSM who continued PrEP in Miami and San Francisco were White, non-Latino MSM (68.3%).¹ These racial disparities echo preliminary findings of a three-site study finding that race was an important factor in predicting lower likelihood of being retained in PrEP care.³ Taken together, these findings suggest that African American and Hispanic/Latino MSM may need culturally tailored case management services to promote optimal rates of retention in care.

There is now a robust body of science supporting PrEP's efficacy.^{10–12} Our scientific and public health agenda for PrEP must change in order to address our nation's alarming rates of racial and ethnic disparities in HIV infection. PrEP studies should move away from a focus on "research in a vacuum" and towards an implementation science agenda that focuses on scaling PrEP in real-world settings.⁹ This agenda should have kept focus on retaining young African American and Hispanic/Latino MSM in PrEP care. Lastly, to avoid precipitous declines in retaining high-risk patients in important PrEP services, PrEP-related research studies should develop plans to seamlessly transition patients from research to clinical care services; one way to facilitate this is to embed research studies in the growing number of PrEP programs that have been established around the country. The research agenda should also take into account evolving changes in the Affordable Care Act and its impacts on PrEP patient care and access to medications and PrEP services, which vary dramatically by state and clinical setting. Far greater efforts are needed to integrate PrEP services into primary care programs, STD clinics and federally qualified health centers.

Important federal policy changes could enhance PrEP outcomes for young MSM of color. Historically, the Ryan White HIV/AIDS Program has been reserved for providing care services for people living with HIV. There is a nascent movement that calls for changes to the program to use Ryan White resources to finance PrEP care services for individuals who are HIV-negative but who are at high risk for HIV acquisition. Many Ryan White-supported clinics now provide PrEP services with non-Ryan White funding sources; allowing some Ryan White resources to be utilized for high-risk HIV negative individuals, in a limited manner, could bolster retention in PrEP care. Additionally, the Centers for Disease Control and Prevention has a longstanding policy against purchasing pharmaceuticals, with limited exceptions. In the President's budget request for Fiscal Year 2017, however, the Administration proposed a small demonstration project that would have permitted state health departments to use a small part of their federal HIV prevention funding for PrEP medications. While the continuing resolution that will control federal funding for the remainder of this fiscal year did not enact this demonstration, the policy idea remains relevant as policymakers attempt to remove a range of structural barriers that undermine access to PrEP and related services.

PrEP has the potential to dramatically reduce HIV acquisition among MSM in the United States. However, PrEP's ability to have demonstrable impacts on the epidemic hinges on its optimal implementation in clinical settings that serve young African American and Hispanic/Latino MSM. Our research agenda must now move from efficacy towards translational science focused on promoting PrEP uptake and optimizing retention in care for young MSM of color in real-world settings.

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