

# Pre-exposure Prophylaxis Persistence Is a Critical Issue in PrEP Implementation

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(See the Major Article by Serota et al on pages 574–82.)

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Pre-exposure prophylaxis (PrEP) is a highly effective tool that has the power to revolutionize the human immunodeficiency virus (HIV) prevention toolbox, with use rising among US men who have sex with men (MSM) [1–3]. Rapid, subsidized, PrEP implementation among key populations can dramatically reduce HIV incidence, even in populations with high HIV treatment coverage [2]. However, disparities remain, with less PrEP use among black MSM and youth, particularly in the Southeastern United States, populations with disproportionate HIV incidence [3]. Uptake is even lower among women and people who inject drugs [3]. The high adherence and retention in care seen in early PrEP demonstration projects [4] has not been sustained among later PrEP adopters within routine clinical settings, with 37–62% discontinuing PrEP by 6 months [5–7]. Higher rates of PrEP discontinuation among youth and black MSM, observed across multiple studies [4, 5], are likely to only amplify disparities in the HIV epidemic. PrEP persistence, or sustaining

PrEP use over time, has become a critical issue in PrEP implementation.

Although PrEP starts can be readily measured by health departments and other agencies, it is more challenging to measure continued use, despite its importance to PrEP's impact, with limited data on PrEP persistence available [3]. Well-designed cohorts, with the ability to measure PrEP starts and stops through close contact with participants, are an important tool to understanding PrEP persistence. In this issue of *Clinical Infectious Diseases*, Serota and colleagues present data on PrEP uptake and discontinuation among young black MSM (YBMSM; aged 16–29 years) in the EleMEnt longitudinal cohort, enrolled in Atlanta, Georgia. EleMEnt was originally designed to examine the relationship between substance use and HIV/sexually transmitted infection (STI) incidence. YBMSM were recruited on the basis of reporting at least one male partner in the prior 3 months, with 298 enrolling in the study. Importantly, study recruitment was not predicated on PrEP interest, nor was there a requirement for high levels of behavioral risk. With the approval of PrEP in 2012, the study obtained PrEP supplemental funding for coverage of provider visits, laboratory testing, travel to clinic visits, and financial navigation to obtain PrEP coverage through available benefit programs. Almost all participants who elected to start PrEP received it free of charge, and all participants were offered

PrEP regardless of meeting Centers for Disease Control and Prevention (CDC) risk criteria for PrEP, because of the relative insensitivity of these measures for HIV risk in this demographic population [8].

In spite of 75% of participants reporting condomless anal intercourse, and almost all being able to receive PrEP for free, only 44% initiated PrEP over the 2-year study. Furthermore, one-quarter waited more than 9 months to start PrEP despite PrEP education and offer at every visit. Although 44% is a substantial increase from the 6% taking PrEP at baseline, the cohort experienced 23 incident HIV infections for an HIV incidence of 5.2/100 person-years (P-Y). For comparison, the HIV incidence in the placebo arm of iPrEx, the first PrEP trial to show efficacy, was 3.9/100 P-Y [1]. Although the HIV incidence was 8.1/100 P-Y in those who never started PrEP, it remained 3.2/100 P-Y in those who had started PrEP at some point throughout the study. These findings illustrate not just limited PrEP uptake in a population with very high HIV incidence but also limited coverage of sexual exposures in those who started PrEP. In fact, the positive predictive value of self-reported adherence to PrEP in the study was only 44%, based on measuring protective drug levels. Furthermore, discontinuations were frequent and multiple, with two-thirds experiencing at least 1 discontinuation. The authors note that the services available to support

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PrEP initiation and persistence in this cohort exceed those in routine clinical setting; hence the findings observed are likely optimistic of what could be expected in general medical care.

The high number of discontinuations and reinitiations observed has important implications for PrEP programs. Although the study endeavored to provide same-day PrEP starts when clinicians were available, some participants waited 1–2 weeks for a PrEP intake, which is still likely much faster than many experience in routine clinical care [9]. Streamlined processes for starting and restarting PrEP likely improve PrEP outcomes. Individuals who were eligible for same-day PrEP starts in New York City STI Clinics were more likely to initiate PrEP, and individuals who start PrEP faster are more likely to remain on PrEP [9, 10]. The availability of same-day or rapid PrEP starts leverage critical moments when motivation to start PrEP is likely to be at its highest. Finally, “on-demand” or “2-1-1” PrEP may be attractive to those ambivalent about daily PrEP use, particularly given the ability to restart PrEP as little as 2 hours prior to a planned sexual exposure [11].

The association seen in this study between positive urine drug screens for stimulants and PrEP discontinuation echoes findings in other studies [12]. However, it should be noted that stimulant users can achieve high adherence to PrEP over time [12]. Stimulant use should not be a deterrent for providers to prescribe PrEP, and PrEP should be offered in addition to substance use treatment and harm reduction strategies. The association between heavy cannabis use and PrEP discontinuation is intriguing and merits additional study.

Although we might expect those with fewer sexual partners to have higher rates of discontinuation, as observed in EleMent, it should be noted that other cohorts have demonstrated high HIV incidence in those stopping PrEP, including those who do so in the context of perceived lower risk [13, 14]. The focus on

behavioral risk criteria in US PrEP roll-out may discount the importance of sexual networks in impacting HIV risk, as many YBMSM appear to be at substantial risk of HIV despite having few sexual partners [8]. PrEP guidelines should be revised to incorporate HIV epidemiologic data in determining who are good PrEP candidates, as a focus solely on risk may reinforce PrEP stigma [15], in addition to predicting HIV risk poorly in populations such as YBMSM [8].

The association between STI diagnosis and PrEP discontinuation is troubling. The authors report that a related qualitative study revealed one potential mechanism, as some participants reported that an STI diagnosis was a signal to “slow down” their sexual activity, with some attributing their STI diagnosis to their PrEP use. Alternatively, an STI diagnosis may reinforce the stigma that also limits PrEP uptake and persistence. Continued investment and development of new prevention strategies for STIs will likely be needed to achieve the full impact of HIV prevention strategies.

The EleMent study provides important insights for the challenges ahead in maximizing PrEP’s prevention potential. Continued research into navigation strategies, counseling, and decision tools to increase PrEP uptake; and mHealth strategies, telemedicine, express lanes, and pharmacy-delivered PrEP to support PrEP persistence and adherence are urgently needed [16–18]. Continued advocacy for health coverage to support PrEP access, as well as reduced medication costs, is also essential. Serota et al’s finding that that repeated offers increase the chance of PrEP initiation is a reminder of the importance of the repeated and sustained efforts needed to support PrEP use among those who can benefit if we hope to fulfill PrEP’s potential.

## Notes

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