

# Needed: A Life Course Perspective on Maintaining Pre-exposure Prophylaxis Use

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(See the Major Article by Huang et al on pages 379–85.)

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Human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP) has revolutionized HIV prevention. Clinical trials and open-label studies have established that PrEP reduces HIV transmission by 99% for patients adherent to daily dosing [1–3]. Reflecting this development, the 2019 US government campaign to address HIV is termed “End the Epidemic” and has goals of reducing new HIV infections by 75% within 5 years and by 90% within 10 years [4]. Over the past 3 years, the number of PrEP-prescribing clinics in a national database increased from 1200 to more than 2000, although geographic barriers to care remain [5, 6]. Most important, PrEP use has grown substantially, with >50% estimated annual percent increases in use nationally for each year from 2012 through 2017 [7]. In the fourth quarter of 2017, more than 100 000 people in the United States were using PrEP [8]. Research on PrEP is also burgeoning. A search of PubMed identified more than 20 times as many article abstracts citing HIV PrEP in 2019 compared with 2009, 944 vs 42 (see Supplement for

search terms and results). Attention to maintaining use of PrEP among those who have started it has also increased greatly. The search identified 3 abstracts regarding PrEP persistence in care (or retention) in 2009 and 90 abstracts to date in 2019.

Retaining individuals at high risk for HIV transmission in PrEP care is essential for PrEP to have a substantial impact on the epidemic. The excellent article by Huang et al in this issue of *Clinical Infectious Diseases* measures persistence in PrEP care in 2 samples: a commercial insurance claims database and a Medicaid enrollee database, each representing about one-fifth of enrollees with each type of coverage. Findings from the commercial dataset are similar to those from an analysis I led using national pharmacy chain data [9]. In both datasets, almost half of commercially insured persons failed to maintain PrEP use a year later, and falloff from PrEP care continued at relatively high rates into the second year of care. Factors correlated with persistence in care were also similar between the 2 studies, with younger persons, females, and those with government-provided health insurance less likely to be retained in PrEP care. This indicates that the major findings of the studies replicate across different samples and that slightly different definitions of persistence in PrEP care do not appear to impact the primary findings.

Huang et al add to the previous literature by including an analysis that broke

down Medicaid data by race. They identified a negative univariate association between being black and persistence in care, although this relation was not significant in multivariate analyses that adjusted for sex and age. Huang et al also revealed a large disparity in length of PrEP persistence between those with Medicaid coverage (median, 6.8 months) and those with commercial insurance (median, 13.7 months), a nearly 2-fold difference. Given available data, it is unclear if some component of Medicaid coverage is directly causing low persistence or if Medicaid coverage is a proxy for other factors correlated with the outcome, such as income, education, or transportation access.

As noted by the authors, their analysis is limited in several ways. The commercial insurance database oversamples higher-income individuals, potentially leading to overestimation of persistence in care, and of the difference between commercial and Medicaid users. The extent of bias this sampling issue introduces remains to be explored. PrEP reinitiation was not assessed, leading to some level of underestimation of persistence in care. On the other hand, restricting the analysis to individuals with a full year of previous continuous health insurance coverage likely led to some overestimation.

Most striking, however, even in the highest persistence group in Huang et al's analysis, median persistence on PrEP was less than 2 years (18.9 months). Such levels of retention probably are

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insufficient to achieve the goals of the “End the Epidemic” initiative. Two modeling studies based on different datasets found that longer periods of persistence in PrEP care had substantial impact on incident HIV infection [10, 11]. Further modeling using updated national persistence data could indicate the likely impact of varying levels of retention in PrEP care on meeting national targets.

Specifying the optimal period of time on PrEP is difficult because some individuals appropriately cycle out of PrEP care when they exit “seasons of risk” [12]. However, the half-year median persistence time of PrEP among Medicaid users is almost certainly too short for optimal outcomes. Indeed, such short periods of protection may defeat the overall purpose of PrEP, and it is not plausible that sweeping changes in sexual risk occurred for half of the persons in this group. In fact, 2 cohort studies have documented substantial HIV incidence among persons discontinuing PrEP [13, 14]. Reasons cited for cessation of PrEP care vary broadly both within and between studies: stigma, transportation barriers, the burden of quarterly clinic visits, insurance coverage changes, perceived HIV risk, mental health issues, medication side effects, new relationships, and more [13, 15–19]. Thus, a single solution is unlikely to resolve PrEP cessation issues. Future interventions should benefit from a multifaceted approach.

The brevity of persistence in PrEP care documented in this and previous studies points to a need to learn what happens to people who stop using PrEP. For many persons, HIV risk will initiate in their teens and continue through much of their life course, so it is imperative to document PrEP use over longer periods. To date, nearly all PrEP studies have at most a 2-year follow-up period. Characterizing patterns of uptake and discontinuation over longer time periods will be critical. These changes should be

tied to HIV incidence in order to understand their potential epidemic ramifications, and studies should explore the impact of different life stages on PrEP use. A life course perspective brings in other relevant factors for consideration, such as policies that may facilitate PrEP use and medical mistrust that may inhibit it. Length and consistency of past PrEP use, ease of access to PrEP, and frequency of offers from clinicians may impact PrEP retention over the times in which persons are at risk for HIV. Better understanding these and other relevant factors will facilitate development of appropriate interventions to improve PrEP delivery and support over the lives of people who can most benefit from its protection.

## Notes

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