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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References

1. Anderson PL, Glidden DV, Liu A, et al; iPrEx Study Team. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med* 2012; 4:151ra125.
2. Grant RM, Lama JR, Anderson PL, et al; iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; 363:2587–99.
3. Grant RM, Anderson PL, McMahan V, et al; iPrEx Study Team. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *Lancet Infect Dis* 2014; 14:820–9.
4. CDC Foundation. Episode 7, On the Frontlines of Public Service. Available at: <https://www.cdcfoundation.org/conversations/robert-redfield>. Accessed 26 December 2019.

5. Siegler AJ, Wirtz S, Weber S, Sullivan PS. Developing a web-based geolocated directory of HIV pre-exposure prophylaxis-providing clinics: the PrEP locator protocol and operating procedures. *JMIR Public Health Surveill* 2017; 3:e58.
6. Siegler AJ, Bratcher A, Weiss KM. Geographic access to preexposure prophylaxis clinics among men who have sex with men in the United States. *Am J Public Health* 2019; 109:1216–23.
7. Sullivan PS, Giler RM, Mouhanna F, et al. Trends in the use of oral emtricitabine/tenofovir disoproxil fumarate for pre-exposure prophylaxis against HIV infection, United States, 2012–2017. *Ann Epidemiol* 2018; 28:833–40.
8. Siegler AJ, Mouhanna F, Giler RM, et al. The prevalence of pre-exposure prophylaxis use and the pre-exposure prophylaxis-to-need ratio in the fourth quarter of 2017, United States. *Ann Epidemiol* 2018; 28:841–9.
9. Coy KC, Hazen RJ, Kirkham HS, Delpino A, Siegler AJ. Persistence on HIV preexposure prophylaxis medication over a 2-year period among a national sample of 7148 PrEP users, United States, 2015 to 2017. *J Int AIDS Soc* 2019; 22:e25252.
10. Jenness SM, Maloney KM, Smith DK, et al. Addressing gaps in HIV preexposure prophylaxis care to reduce racial disparities in HIV incidence in the United States. *Am J Epidemiol* 2019; 188:743–52.
11. Chan PA, Goedel WC, Nunn AS, et al. Potential impact of interventions to enhance retention in care during real-world HIV pre-exposure prophylaxis implementation. *AIDS Patient Care STDS* 2019; 33:434–9.
12. Pines HA, Gorbach PM, Weiss RE, et al. Sexual risk trajectories among MSM in the United States: implications for pre-exposure prophylaxis delivery. *J Acquir Immune Defic Syndr* 2014; 65:579–86.
13. Serota DP, Rosenberg ES, Sullivan PS, et al. Pre-exposure prophylaxis uptake and discontinuation among young black men who have sex with men in Atlanta, Georgia: a prospective cohort study. *Clin Infect Dis* 2019. doi:10.1093/cid/ciz894
14. Krakower D, Maloney KM, Powell VE, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc* 2019; 22:e25250.
15. Hojilla JC, Vlahov D, Crouch PC, Dawson-Rose C, Freeborn K, Carrico A. HIV pre-exposure prophylaxis (PrEP) uptake and retention among men who have sex with men in a community-based sexual health clinic. *AIDS Behav* 2018; 22:1096–9.
16. Dombrowski JC, Golden MR, Barbee LA, Khosropour CM. Patient disengagement from an HIV preexposure prophylaxis program in a sexually transmitted disease clinic. *Sex Transm Dis* 2018; 45:e62–4.
17. Chan PA, Mena L, Patel R, et al. Retention in care outcomes for HIV pre-exposure prophylaxis implementation programmes among men who have sex with men in three US cities. *J Int AIDS Soc* 2016; 19:20903.
18. Arnold T, Brinkley-Rubinstein L, Chan PA, et al. Social, structural, behavioral and clinical factors influencing retention in pre-exposure prophylaxis (PrEP) care in Mississippi. *PLoS One* 2017; 12:e0172354.
19. Rusie LK, Orengo C, Burrell D, et al. Preexposure prophylaxis initiation and retention in care over 5 years, 2012–2017: are quarterly visits too much? *Clin Infect Dis* 2018; 67(2): 283–7.