Long-term HIV Pre-exposure Prophylaxis Trajectories Among Racial & Ethnic Minority Patients: Short, Declining, & Sustained Adherence

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Background: HIV pre-exposure prophylaxis (PrEP) requires continued use at an effective dosage to reduce HIV incidence. Data suggest early PrEP drop-off among many populations. We sought to describe PrEP use over the first year among racial and ethnic minority patients in the US.

Setting: Racial and ethnic minority patients initiating PrEP at a federally qualified health center in Chicago, IL.

Methods: Using electronic health records, we determined the adherence (≥6 weekly doses) trajectories over the first year of PrEP use and compared baseline and time-varying patient characteristics.

Results: From 2159 patients, we identified 3 PrEP use trajectories. Sustained use was the most common (40%) trajectory, followed by short use (30%) and declining use (29%). In adjusted models, younger age, Black race, as well as gender, sexual orientation, insurance status at baseline, and neighborhood were associated with trajectory assignment; within some trajectories, insurance status during follow-up was associated with odds of monthly adherence (≥6 weekly doses).

Conclusion: Among racial and ethnic minorities, a plurality achieved sustained PrEP persistence. Access to clinics, insurance, and intersectional stigmas may be modifiable barriers to effective PrEP persistence; in addition, focus on younger users and beyond gay, cismale populations are needed.

Key Words: PrEP, adherence, persistence, race/ethnicity

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INTRODUCTION

Daily oral HIV pre-exposure prophylaxis (PrEP) is an effective HIV prevention tool.[1,2] To maximize prevention, individuals must take PrEP consistently enough to remain biologically protected, which is measured by adherence, and long enough while potentially exposed to HIV to be protected, which is measured by persistence.[3,4] Adherence and persistence metrics have been inconsistently reported[5,6] but the literature suggests many patients stop using PrEP relatively soon after initiation, particularly among ciswomen and transwomen and racial/ethnic minorities[6–17]; better adherence and persistence are therefore needed to end the HIV epidemic. However, there are also patients who can successfully use PrEP for extended periods of time. There are limited data on patterns of PrEP use over time in the United States (US), which limits our understanding of how patients are adhering and persisting to PrEP and where interventions may be useful, at both individual and structural levels.[9,17–20]

We sought to explore patterns of PrEP use over the first year after initiation specifically among racial/ethnic minority patients of all genders to inform future interventions for these population. Furthermore, we examined patient characteristics and experiences at baseline and over follow-up that differed between PrEP use patterns.

METHODS

We included electronic health record (EHR) data from all Howard Brown Health (HBH) patients who started PrEP 2015–2018 and self-identified as Latinx, Asian, or Black. HBH is a large, federally qualified health center with locations in diverse community areas within Chicago, IL, specializing in sexual health, particularly among sexual and gender minorities. PrEP prescription, insurance status, sexually transmitted infection, and HIV testing data were included for the 12 months after PrEP initiation, censored at HIV seroconversion; HIV results were available for all follow-up time. All available follow-up time was also used to collect PrEP prescription data and calculate total time on PrEP[5]; of note, total time on PrEP is calculated as first prescription until end of the last prescription, and can include gaps in use.

We calculated pills per month available (using proportion of days covered, or PDC) and modeled the outcome as average weekly adherence (per month) at ≥6 doses (≥86% adherence); in a sensitivity analysis, we used average weekly

adherence ≥4 doses (per month).[5] PDC at 6 months is a measure of both adherence and persistence, assessing duration and degree of usage. We also assessed whether patients had a PrEP stop (≥1 month with 0 doses) and among those with a stop, a PrEP restart (≥2 consecutive months with PDC ≥ 86%). Insurance data were updated each time a new insurance carrier was documented in the EHR; if there was no new insurance information, we assumed the prior information was still valid. Demographic information was also collected from the EHR, including age, marital status (dichotomized to partnered or not partnered), self-identified race & ethnicity, sexual orientation, gender identity, and residential zip code. Patient zip code was used to assign patients to Northside, Westside, or Southside residence in Chicago,[21] each with a unique racial and ethnic make-up. Patients with missing race, sexual orientation, or zip code were excluded (n = 844).

Using group-based trajectory models, we modeled monthly adherence as a binary outcome for each month over the first 12 months of PrEP use.[22–26] In group-based trajectory models, each individual is assigned to the trajectory with the highest posterior probability and individuals do not move between trajectories. We tested 2 to 6 trajectories (as is generally recommended), assessing the fit using the Bayes test, group sizes, and posterior probabilities. We then tested linear, quadratic, and cubic terms to find the best fit given the number of trajectories. Spaghetti plots of 200 randomly selected participants per group were plotted to assess whether they were meaningfully different. We tested all baseline variables (using binary dummy variables) to determine associations with trajectory assignment; all significant variables were included in the full model, which also means not all levels of some variables were included in the final model. All time-varying variables (sexually transmitted infection test results and insurance status) were tested to determine any change in the odds of successful adherence (≥6 weekly doses) over time. All significant time-varying variables were also included in the final model. Finally, we present baseline characteristics, PrEP stops and restarts, and HIV seroconversions by adherence trajectory. All analyses were conducted in SAS 9.4. The study was approved and consent waived by HBH and University of Chicago IRBs.

TABLE 1. Participant Characteristics at PrEP Initiation

	Participants (n = 2159)
Age	
18–25	33.8% (730)
26–35	44.1% (953)
36–45	15.4% (333)
46+	6.6% (143)
Race & ethnicity	
Latinx	46.4% (1001)
Asian	12.7% (275)
Black	40.9% (883)
Gender	
Ciswoman	5.2% (112)
Cisman	86.2% (1862)
Transman	1.1% (24)
Transwoman	7.5% (161)
Orientation	
Gay	72.2% (1558)
Lesbian	0.4% (8)
Bisexual	11.0% (239)
Queer	6.8% (147)
Straight	9.6% (207)
Partnered (missing = 222)	85.7% (1660)
Insurance	
Private	46.6% (1005)
Public	21.6% (467)
Self-pay	31.8% (687)
Chlamydia diagnosis	9.7% (210)
Gonorrhea diagnosis	7.2% (155)
Syphilis diagnosis	3.2% (70)
Location	
South Chicago	24.0% (518)
West Chicago	20.9% (450)
North Chicago	55.1% (1190)
Met CDC PrEP criteria (missing = 150)	57.7% (1159)
Year started PrEP	
2015	12.1% (261)
2016	24.5% (529)
2017	34.6% (746)
2018	28.9% (623)

RESULTS

We included data from 2159 patients. A plurality (46%) identified as Latinx, followed by 41% as Black, and 13% as Asian (Table 1). The participants were predominantly cismen (86%), with 8% transwomen and 5% ciswomen; most (72%) identified as gay. This was a young cohort, as one-third were 18–25. Most had started PrEP in 2017 or 2018. The average total time on PrEP was 18.6 months; only 45% had PrEP persistence ≥6 weekly doses consistently over the first 6 months.

Three quadratic trajectories best fit the adherence data (Fig. 1). Group 1, known as short PrEP use, constituted 30% of our sample; this group is characterized by rapid discontinuation of PrEP. Group 3, known as the declining PrEP use, made up 29% of our sample; this group, although more variable, had gradually diminishing adherence over time. Group 2, known as the sustained PrEP use, accounted for 41% of the sample and were characterized by consistently high adherence over the first 12 months.

These 3 PrEP use groups differed by baseline and follow-up characteristics (Table 2). Total time on PrEP (which does not account for gaps or number of doses per month) was 10 months on average for the short PrEP use group, compared with 25.8 months for the sustained PrEP use group. No 1 in the short PrEP use group persisted on PrEP at 6 months at the PDC ≥ 86% threshold, compared with 47% of the declining PrEP use group and 77% of the sustained PrEP use group. Furthermore, 5.4% of the short PrEP use group seroconverted at some point after PrEP initiation (including after the first year of PrEP use), compared with 4% of the declining PrEP use group and 1% of the sustained

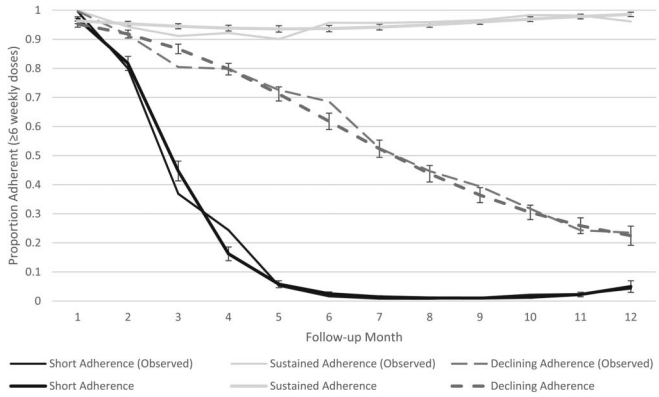

FIGURE 1. Observed and predicted adherence by assigned PrEP use trajectory (95% CI).

PrEP use group. In addition, there were noticeably different patterns of stopping and restarting PrEP by trajectories (see Figure 1, Supplemental Digital Content, http://links.lww.com/QAI/B747). The short use trajectory was characterized by 100% having a PrEP stop and a small percent of those (6%) ever restarted. The declining use trajectory also had a high percentage stopping PrEP (91%) but almost a third of those (35%) ever restarted PrEP. Finally, PrEP stopping was rarest among the sustained use trajectory (9%) and all of these individuals restarted PrEP.

There were also differences in patient characteristics across those assigned to each trajectory (Table 2). Young patients (18–25) comprised 44% of the short use trajectory and 24% of the sustained use trajectory; the reverse pattern was observed for those ages 26–35 and 36–45, with no apparent differences among those 46 and older. Black patients comprised half of the short use trajectory and 32% of the sustained use trajectory; Asian patients, however, were 16% of the sustained use trajectory and 8% of the short use trajectory. In gender and orientation, the sustained use trajectory was predominantly cismen (93%) and identified as gay (81%). There were also differences by insurance status and location, with larger proportions of the sustained use trajectory having private insurance and from the Northside. Finally, there were small differences by chlamydia and gonorrhea diagnosis at PrEP initiation but not by syphilis diagnosis.

From the final model, 2 measures of association can be interpreted. For baseline characteristics, the odds of assignment in one trajectory relative to the sustained PrEP use trajectory are calculated. For time-varying characteristics, the odds of achieving adherence (PDC ≥ 86%, equivalent to ≥6 doses/week) for any month when the event was present versus not present, within each trajectory, is presented. In the final model (Table 3), younger age (18–25) was associated with increase odds of being assigned to the short PrEP use vs sustained PrEP use trajectory {aOR 2.07, 95% confidence interval (CI): [1.63 to 2.63]} and declining vs sustained PrEP use trajectory [aOR 1.60, 95% CI: (1.25 to 2.05)]. Black race was associated with increased odds of short or declining PrEP use vs sustained PrEP use trajectory [aOR 1.48, 95% CI: (1.15 to 1.90); aOR 1.38, 95% CI: (1.08 to 1.78) respectively]. Cismen had lower odds of short or declining PrEP use trajectories, relative to sustained use [aOR 0.71, 95% CI: (0.49 to 1.05); aOR 0.66, 95% CI: (0.44 to 0.98)]. Both bisexual and straight sexual orientations were associated with higher odds of short vs sustained PrEP use trajectories [aOR 1.94, 95% CI: (1.36 to 2.78); aOR 3.86, 95% CI: (2.40 to 6.21), respectively]. Public insurance and self-pay at baseline were associated with increased odds of short vs sustained PrEP use trajectories [aOR 1.65, 95% CI: (1.20 to 2.26); aOR

TABLE 2. Baseline Characteristics by Assigned PrEP Use Trajectory

	Short Use (n = 648)	Declining Use (n = 624)	Sustained Use (n = 891)
Age			
18–25	44.4% (288)	36.9% (230)	23.9% (212)
26–35	37.4% (242)	43.4% (271)	49.6% (440)
36–45	11.7% (76)	13.0% (81)	19.8% (176)
46+	6.5% (42)	6.7% (42)	6.7% (59)
Race & ethnicity			
Latinx	41.1% (266)	43.6% (272)	52.2% (463)
Asian	8.2% (53)	13.3% (83)	15.7% (139)
Black	50.8% (329)	43.1% (269)	32.1% (285)
Gender			
Ciswoman	10.0% (65)	5.1% (32)	1.7% (15)
Cisman	79.0% (512)	84.8% (529)	92.6% (821)
Transman	1.2% (8)	1.3% (8)	0.9% (8)
Transwoman	9.7% (63)	8.8% (55)	4.9% (43)
Orientation			
Gay	60.2% (390)	71.6% (447)	81.3% (721)
Lesbian	0.8% (5)	0.5% (3)	0% (0)
Bisexual	14.7% (95)	11.4% (71)	8.2% (73)
Queer	6.0% (39)	7.5% (47)	6.9% (61)
Straight	18.4% (119)	9.0% (56)	3.6% (32)
Partnered (missing = 222)	14.2% (79)	13.3% (74)	15.0% (124)
Insurance			
Private	31.6% (205)	44.4% (277)	59.0% (523)
Public	28.9% (187)	21.8% (136)	16.2% (144)
SelfPay	39.6% (256)	33.8% (211)	24.8% (220)
Chlamydia diagnosis	11.9% (77)	9.5% (59)	8.3% (74)
Gonorrhea diagnosis	8.2% (53)	8.5% (53)	5.5% (49)
Syphilis diagnosis	3.6% (23)	2.9% (18)	3.3% (29)
Location			
South Chicago	34.0% (220)	23.9% (149)	16.8% (149)
West Chicago	23.2% (150)	23.7% (148)	17.2% (152)
North Chicago	42.9% (278)	52.4% (327)	66.0% (585)
Met CDC PrEP criteria (missing = 150)	56.0% (334)	56.8% (335)	59.6% (490)
Year started PrEP			
2015	12.0% (78)	9.8% (61)	13.7% (122)
2016	22.1% (144)	25.0% (156)	26.0% (232)
2017	34.0% (221)	26.7% (229)	33.7% (300)
2018	32.0% (208)	28.5% (178)	26.6% (237)
Mean total PrEP time in mo (SD)	10.0 (13.0)	17.3 (12.8)	25.8 (11.9)
PDC ≥6 weekly doses at 6 mo	0% (0)	47.3% (295)	76.9% (682)
Ever seroconvert	5.4% (35)	4.0% (25)	1.0% (9)

2.67, 95% CI: (2.06 to 3.47), respectively]; self-pay was also associated with lower odds of declining PrEP use vs sustained [aOR 1.73, 95% CI: (1.29 to 2.32)]. West and Southside residence increased odds of short PrEP use vs sustained trajectories [aOR 1.73, 95% CI: (1.29 to 2.32); aOR 1.79, 95% CI: (1.33 to 2.42), respectively]; Westside was also associated with short vs sustained PrEP use trajectories. During follow-up, among the short PrEP use group, public insurance use decreased odds of adherence [aOR 0.44, 95% CI: (0.21 to 0.91)], whereas public insurance increased the odds of adherence among the declining trajectory [aOR 1.77, 95% CI: (1.07 to 2.93)]. Sliding-scale use (a specific subset of self-pay) was also associated with increase adherence among the short PrEP use group only, aOR 1.26, 95% CI: (1.07 to 1.49). Results were similar when the lower adherence threshold (average ≥4 weekly doses per month) was used.

Discussion

In this analysis of racial and ethnic minority patients using PrEP, we found the largest group were assigned to the sustained PrEP use trajectory (41%), indicating many patients can successfully persist on PrEP. We also identified 2 trajectories with limited PrEP use. Although some drop-off is to be expected as behaviors and partnerships change,[3] the higher seroconversion proportion in these 2 groups suggests improved PrEP persistence could be beneficial.

Low PrEP persistence in real-world settings has been well-documented in the literature.[27] A national sample of veterans (majority White and male) found 40% of patients has high adherence (PDC ≥ 80%) over the first year.[28] Another health care system with a racially-, ethnically-, and gender-diverse population found 38% of patients persisted on PrEP (at any level of adherence) over the first year.[29] One study found, among MSM of all races/ethnicities, 60% "on PrEP" at 6 months.[30] Using a lower threshold of ≥4 weekly doses per month at least 9 out of 12 months, a national pharmacy chain found 57% of men and 34% of women persisted on PrEP after 1 year; there were no data available on other genders or race/ethnicity.[7] Younger age and minority race and/or ethnicity (usually compared with White patients) are often associated with lower adherence.[7,27,28,30] Our results among racially & ethnically diverse patients of all genders, with 45% achieving persistence ≥86% PDC at 6 months, fall within these persistence outcomes. By looking beyond average persistence, we also identified patterns of sustained, successful PrEP use, and rapidly declining use.

We identified baseline characteristics associated with these trajectories. As has been previously demonstrated, younger patients have lower adherence and were more likely to be in the short PrEP use trajectory. Self-identified Black race was associated with the short use trajectory, which could be a proxy for access to health care, stigma, racism, or negative experiences with the health care system.[31–33] Likewise, residential neighborhood was also highly significant, with the Westside (largely Latinx population) and Southside (largely Black population) residents less likely to be in the sustained PrEP use trajectory; this could be related to structural factors, including access to health care and transportation, racism, and intersectional stigma.[31–34] Cismen were more likely to be in the sustained PrEP use trajectory, and bisexual and straight patients in the short PrEP use group, which suggests PrEP awareness and acceptability differ by gender identity and sexual orientation.[35–40] Together, this suggests reducing structural barriers such as insurance and access to health care, and addressing PrEP and HIV stigma in some communities, may help improve PrEP adherence.[41–45] However, our results also show that among those in the short PrEP use trajectory, access to health insurance alone may not be sufficient. More work is needed to understand the barriers around insurance access and changes. Additional interventions may be needed to meet the needs of young PrEP users.[46,47] Finally, if these results are replicated, early, targeted interventions for those in the declining PrEP use group may help improve persistence; more research around restarting PrEP may also identify useful areas for interventions.

TABLE 3. Adjusted Associations With Assigned PrEP Use Trajectories

	Short Use (n = 648) aOR (95% CI)	Declining Use (n = 624) aOR (95% CI)	Sustained Use (n = 891) aOR (95% CI)
Baseline*			
Age 18–25	2.07 (1.63 to 2.53) to $P < 0.001$	1.60 (1.25 to 2.05) to $P < 0.001$	Ref
Black race	1.48 (1.15 to 1.90) to $P = 0.002$	1.38 (1.08 to 1.78) to $P = 0.01$	Ref
Cisman	0.71 (0.49 to 1.05) to $P = 0.08$	0.66 (0.44 to 0.98) to $P = 0.04$	Ref
Bisexual	1.94 (1.36 to 2.78) to $P < 0.001$	1.34 (0.91 to 1.96) to $P = 0.14$	Ref
Straight	3.86 (2.40 to 6.21) to $P < 0.001$	1.66 (0.97 to 2.83) to $P = 0.06$	Ref
Insurance			
Public	1.65 (1.20 to 2.26) to $P = 0.002$	1.20 (0.87 to 1.67) to $P = 0.23$	Ref
Self-pay	2.67 (2.06 to 3.47) to $P < 0.001$	1.72 (1.33 to 2.23) to $P < 0.001$	Ref
West Chicago	1.73 (1.29 to 2.32) to $P < 0.001$	1.65 (1.24 to 2.20) to $P < 0.001$	Ref
South Chicago	1.79 (1.33 to 2.42) to $P < 0.001$	1.34 (0.98 to 1.83) to $P = 0.06$	Ref
Time-varying†			
Public insurance	0.44 (0.21 to 0.91) to $P = 0.02$	1.77 (1.07 to 2.93) to $P = 0.02$	1.40 (0.45 to 4.49) to $P = 0.55$
Sliding-scale	1.01 (0.79 to 1.30) to $P = 0.91$	1.26 (1.07 to 1.49) to $P = 0.006$	0.81 (0.62 to 1.05) to $P = 0.11$

*For baseline variables, these are the odds of being assigned to short or declining use trajectory, relative to the sustained use trajectory.
†For time-varying variables, there are the odds, within a trajectory, of achieving adherence when the event occurred, relative to when it did not occur.

These data came from a clinic in the Midwest with a robust PrEP navigation and retention team; therefore, results may not be generalizable to all populations. We used a high adherence threshold, of an average 6 or more weekly doses consistently each month over the first 6 months; event driven-dosing (2-1-1) and other nondaily regimens were not the standard of care and we are currently collecting data on how often patients used nondaily regimens. However, results with a lower threshold, 4 or more weekly doses consistently over the first 6 months, would capture most nondaily regimens and produce similar results (not reported). If nondaily regimens are more common than we anticipated, some individuals would be assigned to the declining trajectory when they should have been in the sustained trajectory. In line with prevention-effective adherence, we would expect PrEP use to relate to perceived HIV risk; however, neither partner status nor CDC PrEP indications were significantly associated with adherence trajectory. This is a limitation of EHR, as better and time-varying measures of sexual behavior were not available. Likewise, neighborhood of residence may have changed over time, but was only available at baseline. Conversely, we did have data on changes in insurance status; however, these changes may have occurred outside of actual PrEP visits and may be subject to measurement error. We recognize that the racial and ethnic categories used were broad and include important subgroups that we were not able to disaggregate.

In conclusion, many Black, Latinx, and Asian patients using PrEP with consistent, sustained PrEP use over the first 12 months. Further research into early interventions for different trajectories is needed. In addition, resources for younger PrEP users and reductions in structural barriers may improve PrEP persistence and reduce new HIV infections.

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