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Patterns of Pre-exposure Prophylaxis (PrEP) Use in a Population Accessing PrEP in Jackson, Mississippi

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Abstract

Pre-exposure prophylaxis (PrEP) persistence is suboptimal in the United States. In the Deep South, a region with high rates of new HIV diagnosis, patterns of PrEP discontinuation remain unexplored. We evaluated data from a clinic-based PrEP program in Jackson, Mississippi and included patients initiating PrEP between August 2018 and April 2021. We considered patients to have a gap in PrEP coverage if they had at least 30 days without an active PrEP prescription; those who restarted PrEP after 30 days were classified as 'stopped and restarted' and those who never obtained a new PrEP prescription were classified as 'stopped and restart'. Patients without a gap in coverage were considered 'continuously on PrEP'. We estimated median time to first PrEP discontinuation and examined factors associated with time to first PrEP discontinuation. Of 171 patients who received an initial 90-day PrEP prescription; 75% were assigned male at birth and 74% identified as Black. The median time to first discontinuation was 90 days (95% CI90–114). Twenty-two percent were continuously on PrEP, 28% stopped and restarted (median time off PrEP=102 days), and 50% stopped and did not restart. Associations with early PrEP stoppage were notable for patients assigned sex female vs male (adjusted hazard ratio [aHR]=1.6, 95% CI1.0–2.5) and those living over 25 miles from clinic vs. 0–10 miles (aHR 1.89, 95% CI1.2–3.0). Most patients never refilled an initial PrEP prescription to improve persistence and facilitate re-starts are needed.

Keywords Pre-exposure prophylaxis · PrEP · Medication persistence · Prevention

Introduction

Despite growing awareness and adoption of pre-exposure prophylaxis (PrEP) as a critical tool for HIV prevention, persistence on PrEP has been suboptimal in the United States (US). Studies in the US suggest that between 25 and 50% of individuals who start PrEP will discontinue PrEP or disengage from PrEP care within a year of initiating PrEP [1–6], and recent meta-analyzed data suggest that about 40% of individuals initiating PrEP in North America will discontinue within six months [7]. Most data on PrEP persistence are from large cities or locations on the East or West coast, focused on men who have sex with men (MSM), or have been focused in the context of research studies. Less is

known about PrEP persistence patterns and factors associated with disengagement in real-world, clinical settings in the Southern US, particularly the Deep South.

In 2019, Mississippi had the sixth highest rate of new HIV diagnoses among adults [8] and was identified as an area of geographic priority for the Ending the HIV Epidemic Initiative [9]. Rates of PrEP uptake in Mississippi remain lower than those of neighboring southern states with comparable annual rates of new HIV diagnoses [10]. Mississippi also has one of the lowest PrEP-to-Need Ratios (PnR) of all US states, defined as the ratio of the number of PrEP users to the number of people newly diagnosed with HIV in the state [10-12]. To improve PrEP access and uptake in Mississippi, Express Personal Health (EPH), a nurse-run sexual health clinic operated by the University of Mississippi Medical Center and located in Jackson, Mississippi, expanded its focus from HIV and STI testing to include PrEP provision in 2018. The clinic's robust data system provides a unique opportunity to examine PrEP outcomes in a real-world clinical setting. In this retrospective cohort analysis, we aim to describe patterns of PrEP persistence, disengagement, and

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factors associated with disengagement among individuals accessing PrEP in a clinic in Jackson, Mississippi.

Methods

Study Design, Setting, and Population

This is a retrospective cohort study using medical record data from patients attending EPH for PrEP initiation between August 1, 2018 and April 15, 2021. EPH is a nurse-run sexual health clinic operated by the University of Mississippi Medical Center located in Jackson, Mississippi. As one of only a handful of PrEP providers in Mississippi, EPH was originally conceptualized as a clinic that could offer telemedicine visits for PrEP to reduce barriers to ongoing PrEP care. EPH provides PrEP to existing EPH patients and receives referrals from providers throughout the area and from the Mississippi State Department of Health. EPH offers PrEP to all patients, but providers explicitly recommend PrEP to all men who have sex with men and transgender women, and to individuals testing positive for bacterial sexually transmitted infections. Patients presenting for STI screening (chlamydia/gonorrhea, syphilis, HIV, Hepatitis B and C) were tested for HIV with an antigen/antibody (Ag/ Ab) test. Upon receipt of a HIV negative result, the nurse performing the test then provided education to the patient about PrEP and discussed the possibility of starting PrEP. If patients were interested, the clinic followed national guidelines for same-day PrEP [13]. Patients underwent a clinical evaluation for PrEP, were assessed for signs and symptoms of acute HIV, received a laboratory-based Ag/Ab test and creatine (in addition to the patient's other routine STI tests that were done that day). A PrEP navigator then met with patients for further PrEP education and completion of insurance or patient assistance paperwork. Prior to the COVID-19 pandemic (and continuing during the COVID pandemic), patients could have a telehealth visit with the navigator and/ or clinician and receive a PrEP prescription prior to receiving the results of the baseline labs. Patients were given a 3-month PrEP prescription and asked to attend follow-up visits every three months, at which time they received all recommended laboratory tests. Patients were also given the option to conduct follow-up visits via telehealth, whereby they could attend testing-only clinic visits for laboratory testing and the clinician visits were conducted via telehealth. All patients were encouraged to contact the clinic's PrEP navigator to assist with any issues in accessing their medications, or with any questions about PrEP use. Additionally, patients that discontinued PrEP were invited to continue coming to the clinic for STI screening every three months, creating opportunities for re-engagement in PrEP.

Data Collection and Definitions

All data in this analysis come from the clinic's supplemental PrEP REDCap database [14, 15]. Patient demographic and insurance information is collected by the PrEP navigator. Data from the initial clinical evaluation, including laboratory results and whether or not the patient received a PrEP prescription are recorded by the clinician. Information on prescription pick-up (yes/no) and date of prescription pick-up information for each refill are gathered by the PrEP navigator by calling the patients' pharmacy; these data are entered into the database retrospectively. We perform routine monthly quality checks on the dataset to identify missing data; these are resolved monthly.

For this analysis, we considered patients to have "ever disengaged" from PrEP if they had a period of at least 30 days without an active PrEP prescription (i.e., patients who did not have a prescription refill within 30 days of the end of their 90-day prescription were considered to have "ever disengaged"). This definition is in line with other studies of PrEP persistence [16, 17]. We administratively "closed" the dataset on August 15, 2021 to allow for 4 months of follow-up after April 15, 2021. Patients were considered to be continuously on PrEP if they did not have a 30-day gap in their PrEP prescription refill dates during the analysis period and if they had an active PrEP prescription at the end of the study period on August 15, 2021. Patients identified as being at least 30 days overdue for a follow-up visit to refill their prescription, but who were later seen for a prescription refill after this 30-day window were considered to have stopped and later restarted PrEP. Those identified as ever having a 30-day gap in prescription coverage and who did not later re-engage in care at EPH were considered to have stopped PrEP and never restarted. We did not systematically record instances where patients self-reported a discontinuation but had an active PrEP prescription.

Analysis

We describe patient demographic and clinical characteristics for all clients initiating PrEP, those who remained continuously on PrEP throughout the study period, and for those who ever stopped PrEP care. We report the proportion persistent on PrEP at 3, 6, and 12 months (for comparison with other studies) and use Kaplan–Meier survival plots to estimate median time to first PrEP discontinuation overall and stratified by age and sex assigned at birth. Based on our above definitions of PrEP disengagement, these proportions assume that patients receiving a 90-day supply of PrEP who were later identified as disengaging from PrEP care took their medication daily for all 90 days. We used the log-rank test to test for statistically significant differences in timing of patient disengagement. We used chi-square tests to examine differences in the proportion of patients who disengaged by age, sex assigned at birth, transgender identity, race/ethnicity, referral source, geographic distance from clinical site, and method of PrEP payment. We then examined the association of these factors with time to disengagement using Cox proportional hazards regression. In the Cox model, we included the variables described above, which we identified a priori as being potentially associated with PrEP discontinuation. All analyses were conducted using R (version 4.1.2) [18] and RStudio (version 1.2.1335) [19]. This work was undertaken as a program evaluation of EPH operations and is not considered to be human subjects research; thus, individuals did not provide informed consent.

Results

Between August 2018 through April 2021, 171 patients were given an initial PrEP prescription and thus were eligible for inclusion in this analysis. Nearly a third of patients were less than 25 years old, 75.0% of patients were assigned male sex at birth and 73.8% identified as Black (Table 1).

By the end of the study period, 21.6% of patients remained continuously on PrEP, 28.1% of patients stopped PrEP and later restarted, and 50.3% stopped PrEP and never restarted. Among patients aged 17 to 24 years old, 59.3% were found to have stopped PrEP and never restarted compared to 47.1% of those aged 25 to 34 years, and 43.8% of those 35 and older (Table 1). A higher proportion of people assigned female at birth stopped and never restarted compared to those assigned male at birth (60.5% vs. 46.5%), and those who lived over 25 miles from the PrEP clinic were more likely to stop and never restart compared to those who lived within 25 mile of the clinic. Among patients who tested positive for syphilis at the initial clinic visit, 71.4% stopped PrEP and never restarted. Of the 48 patients who stopped PrEP and later restarted, the median time off of PrEP prior to restarting was 102 days (interquartile range 75–229 days).

Figure 1 displays the Kaplan–Meier survival curve for time to first PrEP stoppage. The median time to first PrEP stoppage was 90 days (95% CI 90–114), indicating that a majority of patients never refilled a PrEP prescription after their initial 90-day prescription. The proportion of patients who remained on PrEP at 3 months after initiation was 45.0% (95% CI 38.2%, 53.1%). Timing of first PrEP stoppage stratified by sex at birth is shown in Fig. 2. A higher proportion of those assigned female at birth stopped PrEP at 90 days compared to those assigned male at birth. Individuals aged 35 and older experienced a more gradual disengagement from PrEP compared to those aged 17-24 and 25-34, however these observations were not found to be statistically significant (Fig. 3; log-rank test p=0.12, Chi-square = 5.21, 2 df). At 6 months after PrEP initiation, only 37.9% (95% CI 31.3%-46.0%) of the original cohort remained continuously on PrEP.

Results of bivariate and multivariate Cox proportional hazards regression analyses examining factors associated with first PrEP stoppage are shown in Table 2. In multivariate analysis, those 35 and older were less likely to stop PrEP during the study period (aHR = 0.64, 95% CI 0.38–1.08) compared to those ages 17–24, though this did not meet statistical significance. Patients assigned female at birth were also identified to be more likely to stop PrEP (aHR = 1.60, 95% CI 0.99–2.58). Living over 25 miles away from the PrEP clinic was significantly associated with greater likelihood of PrEP stoppage (aHR = 1.89, 95% CI 1.19–2.99). There were no statistically significant associations between PrEP stoppage and patient referral source or method of PrEP payment.

Discussion

We present several important findings on patterns of PrEP persistence and factors associated with early PrEP stoppage for this population of patients accessing PrEP care in Jackson, Mississippi. We found that less than a quarter of patients remained continuously engaged in PrEP care by the end of the study period and that only 45% remained on PrEP 3 months after initiating PrEP. We also found that nearly 30% of patients who initiated PrEP stopped and later re-started, with a median gap of about three months off of PrEP. These findings highlight the low degree of PrEP retention and persistence in this population, but also suggest that many individuals who stop PrEP may re-start spontaneously at a later date and may do so with a relatively short gap in care. Nonetheless, additional emphasis on eliminating or shortening periods of PrEP stoppage is a critical next step in improving PrEP care.

We found that the median time to first PrEP stoppage was three months, and that only 45% and 38% of patients who initiated PrEP remained on PrEP 3- and 6-months after initiation, respectively. These proportions fall at the lower end of what has been identified in national studies, but is largely in line with other studies in the South. National data suggest that 87% of patients in the US remain continuously engaged in PrEP care three months after initiation, 73% remain persistent at six months [16], and about 56% of patients remained continuously engaged in PrEP one year after initiation [20]. A recent meta-analysis of studies in North America similarly suggests that about 40% of individuals will disengage from PrEP care within 6 months

Table 1 Characteristics of individuals who initiated pre-exposure prophylaxis, remained continuously on PrEP, stopped and later restarted, and stopped and never restarted (N=171)

	Initiated PrEP (N=171)	Continuously on PrEP N=37	Stopped PrEP and Later Restarted N=48	Stopped PrEP and Never Restarted N=86	Chi-square test statistic	p-value
Overall row percent	100%	21.6%	28.1%	50.3%		
Characteristics	N (col %)	N (row %)	N (row %)	N (row %)		
Age in years					6.28	0.19
17–24	54 (31.8)	11 (20.4)	10 (18.5)	32 (59.3)		
25–34	68 (40.0)	12 (17.6)	24 (35.3)	32 (47.1)		
35 and older	48 (28.2)	14 (29.2)	13 (17.1)	21 (43.8)		
Sex assigned at birth					4.10	0.13
Male	129 (75.0)	27 (20.9)	41 (31.8)	60 (46.5)		
Female	43 (25.0)	10 (23.3)	7 (16.3)	26 (60.5)		
Transgender identity					1.58	0.45
Transgender	4 (2.3)	0 (0.0)	2 (50.0)	2 (50.0)		
Cisgender	167 (97.7)	37 (22.2)	46 (27.5)	83 (49.7)		
Race/ethnicity					9.88	0.13
Black, not Hispanic	127 (73.8)	25 (19.7)	35 (27.6)	66 (52.0)		
White, not Hispanic	34 (19.8)	7 (20.6)	13 (38.2)	14 (41.2)		
Other, not Hispanic	4 (2.3)	1 (25.0)	0 (0.0)	3 (75.0)		
Hispanic	7 (4.1)	4 (57.1)	0 (0.0)	3 (42.9)		
Method of PrEP Payment					9.14	0.06
Manufacturer Assistance Program	111 (67.7)	24 (21.6)	26 (23.4)	60 (54.1)		
Medicaid	12 (7.3)	4 (33.3)	2 (16.7)	6 (50.0)		
Private Insurance	41 (25.0)	6 (14.6)	19 (46.3)	16 (39.0)		
STI diagnoses at initial visit ^a						
Syphilis	14 (8.2)	0 (0.0)	4 (28.6)	10 (71.4)	10.9	< 0.01
Chlamydia	17 (9.9)	2 (11.8)	5 (29.4)	9 (52.9)	4.5	0.10
Gonorrhea	16 (9.4)	5 (31.3)	4 (25.0)	7 (43.8)	0.88	0.65
Referral source					11.20	0.08
MSDH Clinic	18 (11.0)	3 (16.7)	3 (16.7)	12 (66.7)		
СВО	14 (8.6)	0 (0.0)	3 (21.4)	11 (78.6)		
Other	102 (62.6)	23 (22.5)	35 (34.3)	44 (43.1)		
EPH	29 (17.8)	8 (27.6)	6 (20.7)	14 (48.3)		
Geographic distance from PrEP clinic ^b		· · ·			11.76	0.02
0–10 miles	94 (55.0)	27 (28.7)	20 (21.3)	46 (48.9)		
11–25 miles	23 (13.5)	4 (17.4)	11 (47.8)	8 (34.8)		
Over 25 miles	54 (31.6)	6 (11.1)	17 (31.5)	31 (57.4)		

CBO Community Based Organization; EPH Express Personal Healthcare; MSDH Mississippi Department of Health; PrEP pre-exposure prophylaxis

Percentages in table calculated using totals that exclude missing values

^aNot all patients had STI testing completed on the date of their initial visit

^bGeographic Distance from PrEP Clinic calculated using patient addresses and UPrEPMS site address

[7]. Among studies focusing on specific regions or cities of the US, continuous engagement in PrEP care at six months after initiation is shown to range from about 30–40% in Atlanta and North Carolina to 76% in Milwaukee [3, 4, 7]. There are several reasons for the low PrEP persistence in this population. It is possible that mechanisms responsible for

the disproportionate burden of HIV diagnoses and mortality in the Deep South may also impact the observed trends identified in this analysis related to PrEP care engagement, including HIV-related stigma, poverty, pervasive systemic racism, healthcare provider bias, higher levels of sexually transmitted infections, and HIV criminalization laws [21,

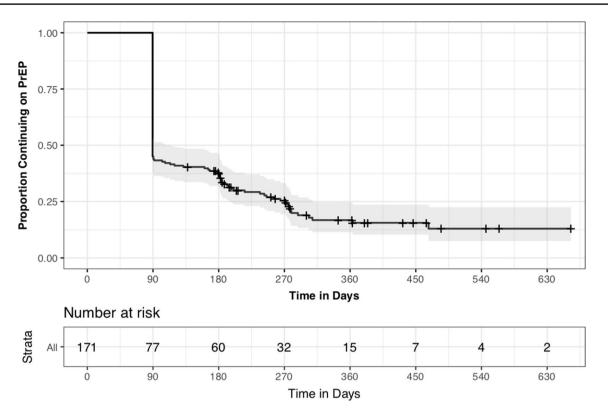
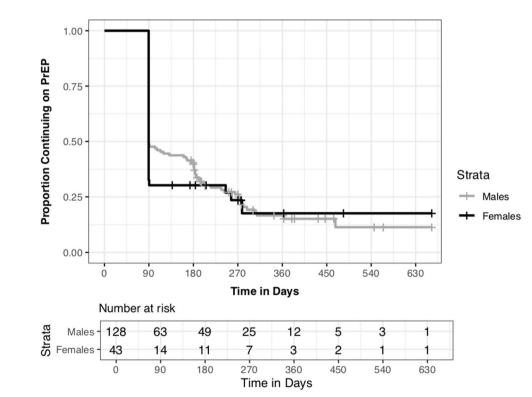
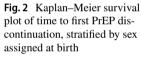
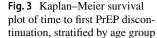
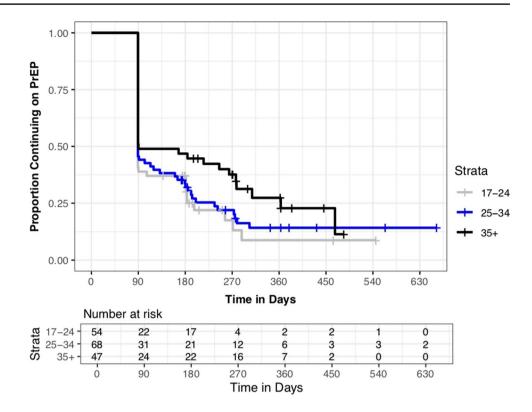


Fig. 1 Kaplan-Meier survival plot of time to first PrEP discontinuation









22]. Second, people who initiate PrEP may later choose to stop taking PrEP for several reasons, such as perceived low HIV risk, side effects, or entering a monogamous relationship with an HIV-seronegative person or a person living with HIV with an undetectable viral load [23]. Previous qualitative work conducted in Jackson, Mississippi identified that major factors affecting PrEP retention included structural factors, such as cost and access to financial assistance for medications and clinical services, social factors, including stigma and relationship status, sexual risk behavioral factors, and clinical factors, such as perceptions and experiences of medication side effects [24]. It is possible that similar factors influenced early PrEP stoppage among the cohort of patients included in this analysis.

Although our analysis focused on time to first PrEP stoppage event, a considerable proportion (28.1%) of patients in this analysis stopped PrEP and later restarted during the study period, a median of 102 days later. This proportion of re-starts is somewhat lower than a study of MSM in Atlanta, which found that 45% of MSM in Atlanta stopped and later restarted PrEP at some point during the study period [17]. However, those data were collected in the context of a research study that provided additional outreach and assistance for study participants, so it is unclear what proportion of patients would re-start PrEP outside the structure of a research study. Notably, tracking PrEP restarts using prescription fill data—as we did here—is challenging. Some patients in this population may have taken PrEP intermittently, stopping and starting as they perceive themselves at risk [25]. Or they may have taken PrEP a few times a week, a dosing schedule that may still be efficacious for HIV prevention [26]. This intermittent PrEP use would have allowed participants to continue to take PrEP beyond the 90-day prescription period and perhaps they did not truly stop and restart PrEP. Nonetheless, we do believe that many patients did indeed have a gap in PrEP coverage. and that additional efforts should be focused on identifying individuals who have stopped PrEP but remain at high risk of acquiring HIV to help decrease the amount of time that individuals have a gap in PrEP coverage. Interventions delivered at the time of PrEP initiation that can decrease structural barriers to re-starts and promote persistence in PrEP care may be useful in settings such as EPH. mHealth and texting interventions, contingency management interventions, and patient navigation interventions have all shown some success in improving PrEP prescription pick-up and/or persistence on PrEP [27-30]. We believe that implementing these interventions as routine practice in our PrEP program is a necessary next-step to improving PrEP persistence.

We found that factors associated with early PrEP stoppage included being between the ages of 17 and 24, being assigned female at birth, and living over 25 miles from the PrEP clinic. These findings are largely consistent with other studies [1, 2, 16, 17]. Younger individuals may face additional challenges in accessing adequate healthcare and may also have fewer experiences navigating PrEP care or any Table 2Bivariate andmultivariable cox proportionalhazard model for First PrEPdiscontinuation (N = 171)

	HR w/ 95% CI	p-value	aHR w/ 95% CI	p-value
	HK W/ 95% CI	p-value	анк w/ 95% Сі	p-value
Age in years				
17–24	Ref	-	Ref	-
25–34	0.90 (0.60, 1.34)	0.60	0.85 (0.53, 1.36)	0.50
35 and older	0.63 (0.40, 1.00)	0.05	0.64 (0.38, 1.08)	0.09
Sex assigned at birth				
Male	Ref	-	Ref	-
Female	1.17 (0.80, 1.75)	0.41	1.60 (0.99, 2.58)	0.06
Transgender identity				
Cisgender	Ref	-	Ref	-
Transgender	1.38 (0.51, 3.75)	0.52	2.50 (0.70, 8.90)	0.16
Race/ethnicity				
Black, not Hispanic	Ref	-	Ref	-
White, not Hispanic	0.78 (0.51, 1.19)	0.24	0.99 (0.58, 1.61)	0.90
Other, not Hispanic	1.38 (0.44, 4.36)	0.59	1.23 (0.58, 1.61)	0.73
Hispanic	0.29 (0.09, 0.91)	0.03	0.33 (0.10, 1.07)	0.07
Method of PrEP Payment				
Manufacturer Assistance Program	Ref	-	Ref	-
Medicaid	0.82 (0.40, 1.70)	0.60	0.74 (0.33, 1.68)	0.47
Private Insurance	1.07 (0.72, 1.58)	0.75	1.01 (0.66, 1.60)	0.96
STI diagnoses at initial visit ^a				
Syphilis	1.63 (0.94, 2.85)	0.08	1.49 (0.76, 2.91)	0.24
Chlamydia	1.64 (0.95, 2.81)	0.07	1.85 (0.93, 3.67)	0.08
Gonorrhea	0.96 (0.52, 1.78)	0.89	0.66 (0.30, 1.46)	0.31
Referral source				
MSDH clinic	Ref	-	Ref	_
CBO	1.41 (0.68, 2.92)	0.36	0.89 (0.39, 2.00)	0.77
Other	0.92 (0.53, 1.61)	0.78	0.84 (0.47, 1.52)	0.57
EPH	0.85 (0.44, 1.66)	0.641	0.74 (0.36, 1.52)	0.42
Geographic distance from PrEP clinic ^b				
0–10 miles	Ref	-	Ref	_
11–25 miles	1.14 (0.68, 1.89)	0.62	1.43 (0.80, 2.58)	0.23
Over 25 miles	1.39 (0.96, 2.02)	0.08	1.89 (1.19, 2.99)	0.007

AHR adjusted hazard ratio; CBO Community Based Organization; CI confidence interval; EPH Express Personal Healthcare; HR hazard ratio, MSDH, Mississippi Department of Health; PrEP pre-exposure prophylaxis

^aNot all patients had STI testing completed on the date of their initial visit

^bGeographic Distance from PrEP Clinic calculated using patient addresses and UPrEPMS site address

healthcare. Providing additional outreach and support for younger PrEP patients may help mitigate PrEP discontinuation. We also noted that early PrEP stoppage was associated with being assigned female at birth, consistent with published findings from similar analyses [1, 2, 16, 19]. While few quantitative studies have directly focused on women in their analyses of PrEP retention, qualitative analyses have identified barriers of limited PrEP knowledge and awareness, HIV-related stigma, financial concerns, and medical mistrust as potential contributors to frequently observed early stoppages among women [31]. Improving understanding of these barriers using an intersectional framework within analyses is also critical; in Mississippi, Black women represented 76% of all new HIV infections among women in 2018 and were nine times more likely than white women to acquire HIV [9]. Lastly, our results identified an association between early PrEP disengagement and living over 25 miles from the clinic site, even though patients had the option of completing visits via telehealth and receiving their medications via mail. This finding suggests that there may be other factors contributing to early PrEP stoppage amongst this group, and enforces the necessity to increase the number and distribution of PrEP providers in both urban and rural communities in order to maximize PrEP coverage in this region of the US.

Strengths of this study include using PrEP prescription refill data (instead of only visits) to monitor PrEP persistence, following patients longitudinally to examine PrEP re-starts after stopping, and examining these important factors in a region of the US with a high burden of new HIV diagnoses. There are also several important limitations to our analysis. First, we are unable to determine the exact date a participant may have stopped taking PrEP. If an individual picked up a 90-day PrEP prescription but did not take their medication, we would erroneously conclude that they had taken PrEP for 3 months. As noted above, it is also possible that some patients took PrEP intermittently and did not truly have a 30-day gap in PrEP coverage as they appeared to in the data. Additionally, the clinic did not systematically document self-reported discontinuation. Therefore, if someone reported discontinuing PrEP but had an active PrEP prescription we would erroneously categorize them as being on PrEP. Anecdotally however, self-reported discontinuation was uncommon. Second, we do not know why individuals stopped PrEP. It is possible that they were truly not at ongoing HIV risk, or that they established PrEP with a different provider in the Jackson area. Although there is a field to document reasons for PrEP discontinuation in our electronic database, this information was rarely filled out. Third, this analysis includes the time period after the start of the COVID-19 pandemic. Many clinics have identified drop-offs in PrEP clinic visits during the initial COVID-19 pandemic [32] though some have observed increases in PrEP visits [33]. Anecdotally, the clinic continued to see PrEP patients with minimal disruption during the COVID-19 pandemic; thus, we do not believe this had a major bearing on our results. Finally, these findings are from a single PrEP provider in Jackson, Mississippi and may not necessarily be generalizable to other settings. This data from a single PrEP provider also limited our overall sample size; the multivariable Cox model estimates must particularly be interpreted with caution, as some of the confidence intervals were relatively imprecise due to the study's limited power.

Our findings suggest that persistence of PrEP among patients seen in this clinic in Jackson, Mississippi was suboptimal, with the median time to first PrEP stoppage occurring three months after initiation and 50% of people never re-starting. These results highlight the need for additional interventions to support patients in continuously engaging in PrEP care, and especially for interventions tailored to meet the needs of younger patients, women, and those living over 25 miles from the clinic. At the same time, our findings also identified that a large proportion of patients will re-start PrEP after stopping, underscoring the need for clinics to streamline PrEP re-starts and to attempt ongoing outreach of those who have stopped PrEP to increase the proportion who re-start. As we continue to move towards the goals of the Ending the HIV Epidemic initiative, identifying ways to improve persistence on PrEP—and not only PrEP uptake—should be an ongoing priority.

Author Contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by EC, LM, KLJ, and MP. The first draft of the manuscript was written by EC and CMK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Code Availability The de-identified data and code are available upon request.

Declarations

Conflict of interest L.M. has received grants from: Gilead Sciences, GSK/ViiV Healthcare, Merck, Roche Molecular, Visby Medical, Binx Health. Evofem Inc, click Dx, Janssen Pharmaceutical, Prosoft Clinical, ThaiMed, SpeedDx Pty LTD., and consulting or advisory fees: from Gilead Sciences, GSK/ViiV Healthcare, Merck, Roche Molecular. C.M.K. has received donations of specimen collection kits and reagents for studies outside the submitted work. All other authors declare no conflicts of interest.

Ethical Approval This analysis was undertaken as a program evaluation of this HRSA-funded program, with the intent for the results to be used to improve the program's operations. Thus, it was exempt from human subjects research approval.

References

- Dombrowski JC, Golden MR, Barbee LA, Khosropour CM. Patient disengagement from an HIV preexposure prophylaxis program in a sexually transmitted disease clinic. Sex Trans Dis. 2018;45(9):e62–4.
- Bruxvoort KJ, Schumacher CM, Towner W, Jones J, Contreras R, Ling Grant D, et al. Referral linkage to preexposure prophylaxis care and persistence on preexposure prophylaxis in an integrated health care system. J Acquir Immune Defic Syndr. 2021;87(3):918–27.
- Hevey MA, Walsh JL, Petroll AE. PrEP continuation, HIV and STI testing rates, and delivery of preventive care in a clinic-based cohort. AIDS Educ Prev. 2018;30(5):393–405.
- Lankowski AJ, Bien-Gund CH, Patel VV, Felsen UR, Silvera R, Blackstock OJ. PrEP in the real world: predictors of 6-month retention in a diverse urban cohort. AIDS Behav. 2019;23(7):1797–802.
- Marcus JL, Hurley LB, Hare CB, Nguyen DP, Phengrasamy T, Silverberg MJ, et al. Preexposure prophylaxis for HIV prevention in a large integrated health care system: adherence, renal safety, and discontinuation. J Acquir Immune Defic Syndr. 2016;73(5):540–6.

- Rusie LK, Orengo C, Burrell D, Ramachandran A, Houlberg M, Keglovitz K, 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.
- Zhang J, Li C, Xu J, Hu Z, Rutstein SE, Tucker JD, et al. Discontinuation, suboptimal adherence, and reinitiation of oral HIV pre-exposure prophylaxis: a global systematic review and metaanalysis. Lancet HIV. 2022;9(4):e254–68.
- Centers for Disease Control and Prevention. *HIV Surveillance Report*, 2019; vol. 32. http://www.cdc.gov/hiv/library/reports/hivsurveillance.html. accessed May 2021.
- STD/HIV Program, Mississippi State Department of Health. Ending the HIV Epidemic in Mississippi: Epidemiologic Profile 2018, Volume 1.
- Siegler AJ, Mouhanna F, Giler RM, et al. The prevalence of preexposure prophylaxis use and the pre-exposure prophylaxis-toneed ratio in the fourth quarter of 2017, United States. Ann Epidemiol. 2018;28(12):841–9. https://doi.org/10.1016/j.annepidem. 2018.06.005.
- PrEP Use Across the U.S. at the County-Level [Internet]. AIDSVu. 2020 [cited 2022 Apr 18]. https://aidsvu.org/ prep-use-across-the-u-s-at-the-county-level/
- Siegler AJ, Mouhanna F, Giler RM, Weiss K, Pembleton E, Guest J, et al. The prevalence of PrEP use and the PrEP-to-need ratio in the fourth quarter of 2017 United States. Ann Epidemiol. 2018;28(12):841–9.
- US Public Health Service: Pre-Exposure Prophylaxis for the Prevention of HIV Infection in the United States—2021 Updates, A Clinical Practice Guideline. 2021;108.
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377–81.
- Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, Delacqua G, Delacqua F, Kirby J, Duda SN. REDCap Consortium, The REDCap consortium: building an international community of software partners. J Biomed Inform. 2019. https:// doi.org/10.1016/j.jbi.2019.103208.
- Huang YLA, Tao G, Smith DK, Hoover KW. Persistence with human immunodeficiency virus pre-exposure prophylaxis in the United States, 2012–2017. Clin Infect Dis. 2021;72(3):379–85.
- 17. Serota DP, Rosenberg ES, Sullivan PS, Thorne AL, Rolle CPM, Del Rio C, 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. 2020;71(3):574–82.
- R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/
- RStudio Team (2022). RStudio: Integrated Development Environment for R. RStudio, PBC, Boston, MA http://www.rstudio.com/.
- 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 Intern AIDS Soc. 2019;22(2): e25252.
- Reif S, Safley D, McAllaster C, Wilson E, Whetten K. State of HIV in the US deep south. J Commun Health. 2017;42(5):844–53.
- 22. Mayer KH, Agwu A, Malebranche D. Barriers to the wider use of pre-exposure prophylaxis in the United States: a narrative review. Adv Ther. 2020;37(5):1778–811.

- 23. Whitfield THF, John SA, Rendina HJ, Grov C, Parsons JT. Why I quit pre-exposure prophylaxis (PrEP)? A mixed-method study exploring reasons for PrEP discontinuation and potential re-initiation among gay and bisexual men. AIDS Behav. 2018;22(11):3566–75.
- 24. Arnold T, Brinkley-Rubinstein L, Chan PA, Perez-Brumer A, Bologna ES, Beauchamps L, et al. Social, structural, behavioral and clinical factors influencing retention in pre-exposure prophylaxis (PrEP) care in Mississippi. PLoS ONE. 2017;12(2): e0172354.
- 25. Vaccher SJ, Gianacas C, Templeton DJ, Poynten IM, Haire BG, Ooi C, et al. Baseline preferences for daily, event-driven, or periodic HIV pre-exposure prophylaxis among gay and bisexual men in the PRELUDE demonstration project. Front Public Health. 2017. https://doi.org/10.3389/fpubh.2017.00341.
- Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med. 2015;373(23):2237–46.
- 27. Liu AY, Vittinghoff E, von Felten P, Rivet Amico K, Anderson PL, Lester R, et al. Randomized controlled trial of a mobile health intervention to promote retention and adherence to pre-exposure prophylaxis among young people at risk for human immunodeficiency virus: the EPIC study. Clin Infect Dis. 2019;68(12):2010–7.
- Fuchs JD, Stojanovski K, Vittinghoff E, et al. A mobile health strategy to support adherence to antiretroviral preexposure prophylaxis. AIDS Patient Care STDS. 2018;32(3):104–11.
- 29. Moore DJ, Jain S, Dube MP, et al. Randomized controlled trial of daily text messages to support adherence to preexposure prophylaxis in individuals at risk for human immunodeficiency virus: the TAPIR study. Clin Infect Dis. 2018;66(10):1566–72.
- 30. Goedel WC, Coats CS, Chan PA, et al. A pilot study of a patient navigation intervention to improve HIV pre-exposure prophylaxis persistence among black/African American men who have sex with men. J Acquir Immune Defic Syndr. 2022;90(3):276–82.
- 31. Willie TC, Monger M, Nunn A, Kershaw T, Stockman JK, Mayer KH, et al. "PrEP's just to secure you like insurance": a qualitative study on HIV pre-exposure prophylaxis (PrEP) adherence and retention among black cisgender women in Mississippi. BMC Infect Dis. 2021;21(1):1102.
- Rogers BG, Tao J, Maynard M, Chu C, Silva E, Toma E, et al. Characterizing the impact of COVID-19 on pre-exposure prophylaxis (PrEP) care. AIDS Behav. 2021;25(11):3754–7.
- Hill BJ, Anderson B, Lock L. COVID-19 pandemic, pre-exposure prophylaxis (PrEP) care, and HIV/STI testing among patients receiving care in three HIV epidemic priority states. AIDS Behav. 2021;25(5):1361–5.

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