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Pre-exposure Prophylaxis Uptake and Discontinuation Among Young Black Men Who Have Sex With Men in Atlanta, Georgia: A Prospective Cohort Study

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Background. Human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP) has great potential to reduce HIV incidence among young black men who have sex with men (YBMSM); however, initiation and persistence for this group remain low. We sought to understand the patterns and predictors of PrEP uptake and discontinuation among YBMSM in Atlanta, Georgia.

Methods. PrEP was offered to all participants in a prospective cohort of YBMSM aged 18–29 years not living with HIV. Time to PrEP uptake, first discontinuation, and final discontinuation were assessed using the Kaplan-Meier method. Cox proportional hazard models were used to identify predictors of uptake and discontinuation.

Results. After 440 person-years of follow-up, 44% of YBMSM initiated PrEP through the study after a median of 122 days. Of PrEP initiators, 69% had a first discontinuation and 40% had a final discontinuation during the study period. The median time to first PrEP discontinuation was 159 days. Factors associated with PrEP uptake included higher self-efficacy, sexually transmitted infection (STI), and condomless anal intercourse. Factors associated with discontinuation included younger age, cannabis use, STI, and fewer sex partners. HIV incidence was 5.23/100 person-years (95% confidence interval [CI], 3.40–7.23), with a lower rate among those who started PrEP (incidence rate ratio, 0.39; 95% CI, .16–.92).

Conclusions. Persistent PrEP coverage in this cohort of YBMSM was suboptimal, and discontinuations were common despite additional support services available through the study. Interventions to support PrEP uptake and persistence, especially for younger and substance-using YBMSM, are necessary to achieve full PrEP effectiveness.

Clinical Trials Registration. NCT02503618.

Keywords. PrEP; MSM; young black men who have sex with men; substance use; cannabis use.

Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) with daily tenofovir/emtricitabine (TDF/FTC) is highly efficacious; however, implementation in the United States has been inequitable. African Americans account for 44% of new HIV infections but make up only 11% of those who receive a prescription for PrEP [1–3]. There is also a geographic disparity in the implementation of PrEP where the South has the highest incidence of HIV and the lowest use of PrEP compared with other regions [4]. HIV incidence is high among young black men who have sex with men (YBMSM), and YBMSM make up the largest number of people with an indication for PrEP in the United States [5] and are most likely to benefit from PrEP [6].

While much of the current drive to end the HIV epidemic has focused on increasing PrEP access and uptake, persistence is equally important for achieving population-level effectiveness of PrEP [7]. PrEP persistence is consistently lower in real-world studies compared with clinical trials and demonstration projects [8, 9]. Younger age and black race have been associated with lower rates of PrEP uptake, lower adherence, and higher rates of discontinuation [10–13]. Some factors that contribute to lower PrEP use among YBMSM include a higher burden of systems barriers, such as lack of awareness and access to PrEP, stigma, discrimination, racism, homophobia, low perceived HIV risk, medical mistrust, and low levels of self-efficacy, which are amplified among YBMSM in the southern United States [14–18].

Understanding the patterns and determinants of PrEP uptake and discontinuation among YBMSM is integral to reducing HIV incidence in this key population. Our objectives were to identify factors that contribute to PrEP uptake and discontinuation among YBMSM enrolled in an observational cohort study with free access to PrEP services. We previously reported factors associated with PrEP uptake in the cohort after approximately

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50% enrollment [19]. Here, we report similar uptake data with the full cohort enrolled and follow-up completed. Among those who initiated PrEP, we sought to describe predictors of PrEP discontinuation, time to discontinuation, and total time on PrEP to better understand persistence and patterns of use.

METHODS

Study Design

The EleMENt study was a longitudinal cohort of YBMSM in Atlanta, Georgia, designed to evaluate the relationship between substance use and HIV/sexually transmitted infection (STI) incidence (NCT02503618). Eligible participants were non-Hispanic black cis-gender men aged 16–29 years in the Atlanta Metropolitan Statistical Area who reported ≥1 male sexual partner in the 3 months before enrollment. Participants without HIV were followed prospectively with 6 study visits over 24 months. At each study visit, participants received risk-reduction counseling, HIV/STI screening, urine drug screening (UDS), and offers of PrEP as outlined below. Participants diagnosed with HIV or STIs were linked to treatment. They also completed computer-administered surveys on demographics, substance use, sexual behaviors, and mental health. Participants were compensated for study visits, and complementary transportation was available if needed. The Emory University Institutional Review Board reviewed and approved the study.

Optional PrEP Program

At each study visit, all participants received PrEP education and were offered enrollment in an optional PrEP program, which has been previously described [19]. Any participant could initiate PrEP irrespective of meeting Centers for Disease Control and Prevention (CDC) guideline indications to initiate because these criteria are an insensitive marker of HIV risk among YBMSM [20]. Interested participants were scheduled to meet with a study clinician in order to assess medical eligibility and provide counseling on how to use daily PrEP. Insured participants were given a prescription for TDF/FTC and a copay assistance card. Uninsured participants obtained PrEP using the manufacturer assistance program (MAP). Study staff collected the required documents and helped participants to complete and submit forms for the MAP and prior authorizations. Almost all participants ended up receiving PrEP for free based on these funding methods. Participants were contacted regularly after their PrEP clinician visit to ensure they had successfully obtained TDF/FTC and to be helped if they had not.

Participants in the PrEP program were monitored with laboratory testing including an HIV rapid test, qualitative HIV nucleic acid test, STI screening, and creatinine every 3–6 months, per CDC guidelines [21]. At each visit after starting PrEP, counselors assessed adherence, side effects, and difficulties obtaining TDF/FTC. Clinical services, laboratory monitoring, and navigation were provided for free through grant funding; however, medication was not provided directly through the study. Participants received no compensation for PrEP program visits, although PrEP visits sometimes occurred at the same time as the incentivized main EleMENt study visit.

Outcomes

PrEP uptake was defined as the date of taking a first dose of TDF/FTC and was assessed approximately 1 month after the clinician visit. If a participant had not initiated PrEP at the 1-month call, staff helped mitigate barriers to initiation and called regularly to assess for initiation. After initiation, PrEP persistence was assessed using a variety of methods, including self-reported adherence at each follow-up visit, telephone call and text message logs, prescription dates, MAP expiration dates, and pharmacy refill records (when available). For each participant who started PrEP, we created a timeline of contact points following initiation and ascertained whether they were on or off PrEP during these time intervals (Supplementary Figure 1).

PrEP discontinuation was defined as ≥14 days off of PrEP after initiation, based on pharmacodynamic data that indicated that protection from HIV was low by 14 days after the last dose [22]. We conducted sensitivity analyses for time to first discontinuation using a more conservative definition of discontinuation, that is, ≥30 days. Because many participants who discontinued PrEP eventually restarted, we also evaluated final discontinuation, which was defined as the last date a participant took PrEP without restarting before the study ended. For participants with an uncertain PrEP discontinuation date, we estimated the discontinuation date to be halfway between their last known date on PrEP and the date we ascertained they were off PrEP. Among participants who discontinued PrEP and never restarted, surveys, charts, and contact logs were evaluated to assess the primary reason for their discontinuation. For HIV incidence, the date of infection was estimated to be halfway between the last negative test and the first positive test.

Covariates

All predictors of uptake and discontinuation, including demographics, sexual behavior, mental health, and substance use, were assessed at the baseline visit. We evaluated different age classifications on the outcomes. The Alcohol Use Disorders Identification Test was used to assess risky alcohol consumption [23]. Substance use was established by creating a composite variable of self-report (used substance within the past 6 months) or UDS positivity. Depression and anxiety symptoms were defined as moderate to severe symptoms using the Patient Health Questionnaire-8 [24] and the Generalized Anxiety Disorder-7 [25]. STI history was a composite variable of either a positive baseline test for syphilis, gonorrhea, or chlamydia or self-report of STI in the past 12 months.

Statistical Analyses

We summarized survey and laboratory data descriptively for the entire cohort. For the PrEP uptake model, participants who reported already being on PrEP at baseline (from a provider outside the study) were excluded. Participants who switched their PrEP care to the study were included in the discontinuation models. A cumulative incidence plot using the Kaplan-Meier method was created to show the time to PrEP initiation. A Cox proportional hazards model was used to estimate the associations between the predictors of interest and PrEP uptake. For multivariable modeling, we controlled for all variables in the bivariable analyses that were chosen based on known or hypothesized associations with PrEP use. Similarly, Kaplan-Meier survival plots were created for time to a first PrEP discontinuation and time to a final discontinuation. Cox proportional hazards models were used to identify the association between predictors and a first and final PrEP discontinuation. The proportional hazards assumption was assessed by examining plots of ln(ln[S(t)]) as well as evaluating for variable-time interaction terms. Both methods confirmed no gross violations of the proportional hazard assumption.

To determine the percent of time with PrEP coverage among those who started PrEP, we summed all of the person-time on PrEP divided by the total possible person-time on PrEP starting from the date of PrEP prescription for each participant. HIV incidence was calculated for the cohort overall and stratified by whether or not a participant ever started PrEP during the study period. An incidence rate ratio (IRR) to compare PrEP initiators with those who never started PrEP was calculated using Poisson regression. To validate self-report of taking ≥4 doses of PrEP with biomarker-proven adherence, a convenience sample of 105 participants had dried blood spots (DBSs) checked for tenofovir diphosphate (TFV-DP). A TFV-DP level of ≥700 fmol/punch was considered consistent with taking ≥4 doses per week [26]. Data analyses were performed using SAS 9.4 (Cary, NC) and Microsoft Excel 2016 (Redmond, WA).

RESULTS

Between June 2015 and June 2017, 298 participants were enrolled; their baseline characteristics are listed in Table 1. Participants had a median age of 24 years (interquartile range [IQR], 22–27), and 73% identified as gay. More than half had worry about their housing stability, and 45% earned less than $20 000 annually. Moderate to severe symptoms of depression or anxiety were present in 19% and 22%, respectively. In the past 6 months, cannabis was used by 68%, cocaine by 14%, and opioids by 8%. Thirty percent screened positive for risky alcohol use; 77% reported condomless anal sex in the last 6 months; and 42% reported an STI in the last year or were diagnosed with a bacterial STI at baseline.

At enrollment, 19 (6%) participants were taking PrEP and were excluded from the uptake models. Seven of those eventually started PrEP through the study. By the end of the study with 440 person-years of follow-up, 44% (124/279) of participants not taking PrEP at baseline had initiated PrEP. Of the PrEP initiators, 69% had a first discontinuation and 40% had a final discontinuation. Among the 34/52 participants for whom a reason for final discontinuation could be identified, the most common reason was low perceived HIV risk (31%), followed by problems attending visits or picking up medications (13%) and side effects (10%; Table 2). After receiving a prescription for PrEP, the

Table 1. Baseline Characteristics of a Cohort of Young Black Men Living With Human Immunodeficiency Virus Who Have Sex With Men

Characteristic	Overall, N = 298 (%)	Initiated Pre-exposure Prophylaxis, n = 131 (%)
Age at enrollment, median (IQR), y	24 (22–27)	25 (21–27)
18–21	62 (21)	19 (15)
22–25	125 (42)	58 (44)
26–29	111 (37)	54 (41)
More than high school education	220 (74)	101 (78)
Income ≥$20 000 annually	164 (55)	76 (58)
Worry about housing	150 (51)	60 (46)
Homeless in the past 6 months	25 (9)	10 (8)
Uninsured	111 (37)	51 (39)
Arrested ever	99 (34)	48 (37)
Sexual orientation		
Gay	215 (73)	98 (76)
Bisexual	65 (22)	26 (20)
Heterosexual	3 (1)	1 (1)
Other	11 (4)	4 (3)
Anxiety symptoms, moderate to severe[a]	66 (22)	29 (22)
Depression symptoms, moderate to severe[b]	57 (19)	22 (17)
High self-efficacy[c]	219 (76)	108 (84)
Cannabis use[d]	202 (68)	81 (62)
Cocaine use[d]	41 (14)	20 (15)
Illicit opioid use[d]	25 (8)	11 (8)
Stimulant use[d,e]	55 (18)	27 (21)
Alcohol use (risky use: yes/no)[f]	88 (30)	39 (30)
Tobacco use[g]	63 (21)	21 (16)
STI in the past 12 months[h]	126 (42)	66 (50)
Number of anal partners in the past 6 months, median (IQR)	2 (1–4)	2 (1–5)
≤2 anal sex partners in the past 6 months	128 (44)	62 (48)
Condomless anal sex in the past 6 months	229 (77)	110 (84)

Abbreviations: IQR, interquartile range; MDMA, 3,4-methylenedioxymethamphetamine; STI, sexually transmitted infection.

[a]Generalized anxiety disorder-7 scale.

[b]Patient health questionnaire-8 scale.

[c]Answered "exactly true" to "I can always manage to solve difficult problems if I try hard enough."

[d]Composite: self-report of use in the past 6 months or positive urine drug screen at enrollment.

[e]Stimulant use included cocaine, amphetamine, methamphetamine, or MDMA.

[f]Alcohol Use Disorders Identification Test.

[g]"Have you smoked over 100 cigarettes in your lifetime."

[h]Composite: self-report STI in the past 12 months or positive STI test at enrollment.

Table 2. Reasons for Final Pre-exposure Prophylaxis Discontinuation

Reason	N = 52 (%)
Positive HIV test	4 (8)
Not currently at risk for HIV	16 (31)
Dislike taking pills	2 (4)
Side effects intolerable	5 (10)
Logistical problems attending appointments or getting pre-exposure prophylaxis[a]	7 (13)
No reason given[b]	18 (35)

Abbreviation: HIV, human immunodeficiency virus.

[a]Two participants had income that was too high for manufacturer assistance program (MAP) eligibility; 2 required prescription prior authorization, which led to lack of follow-up with pre-exposure prophylaxis; 2 could not secure transportation to pick up prescription at their pharmacy; and 1 failed to submit forms to renew their MAP.

[b]None were lost to follow-up, but no documentation of reason for discontinuation was recorded.

131 participants who started PrEP were taking PrEP 67% of the time, with a start/stop pattern shown in Figure 1. The positive predictive value of self-reported adherence to PrEP for finding protective drug levels was 44% (95% CI, 40%–48%).

HIV Incidence

There were 23 incident HIV infections (5.23/100 person-years; 95% CI, 3.40–7.23). Among the 143 participants on PrEP at baseline or who started PrEP, incidence was 3.15/100 person-years (95% CI, 1.35–6.20). HIV incidence among those who never started PrEP was 8.09/100 person-years (95% CI ,4.53–13.34) (IRR 0.39; 95% CI, .16–.92; $P = .03$).

PrEP Uptake

PrEP uptake occurred after a median of 122 days (IQR, 44–275; Figure 2) among the 124 participants not taking PREP at baseline. Additionally, there were 7 participants on PrEP at baseline who transitioned their care to the study (131 total started PrEP). One-quarter of those who initiated PrEP did so >9 months after their baseline visit. In the multivariable Cox model for PrEP uptake, higher self-efficacy for problem-solving, STI diagnosis, and condomless anal intercourse (CAI) were all associated with increased PrEP uptake (Table 3).

PrEP Discontinuation

Of the 131 participants who started PrEP through the study, the median time to a first discontinuation was 159 days (IQR, 97–237) after taking their first dose of PrEP (Figure 3). In the multivariable model, younger age, cannabis use, STI diagnosis, and fewer sex partners were associated with earlier first PrEP discontinuation (Table 4). When the cannabis use variable was further broken down into frequency of use, the cannabis/discontinuation association was accounted for by daily users only (Supplementary Table 1). Additionally, while there was no association between the composite measure of stimulant use and discontinuation, having a stimulant-positive UDS was associated with discontinuation of PrEP. Using a 30-day cutoff for

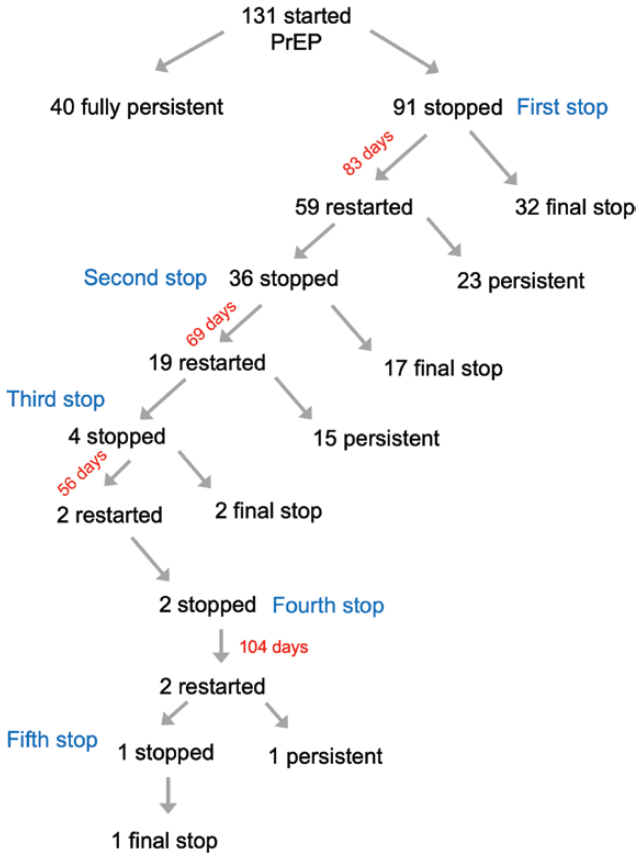

Figure 1. Pattern of pre-exposure prophylaxis (PrEP) discontinuation among young black men who have sex with men. Tree diagram represents the patterns of discontinuations and restarts among 131 participants who initiated PrEP. Each discontinuation represents ≥14 days off of PrEP. The median time (in days) to reinitiation is presented.

PrEP discontinuation, 62% had a first discontinuation after a median of 165 days (IQR, 97–243). There was no difference between the 14-day and 30-day survival curves (log-rank test, $P = .15$).

The median time to final discontinuation was 223 days (IQR, 130–395; Figure 3). Similar to first PrEP discontinuation, younger age, cannabis use, and fewer sex partners, but not STI, were associated with final PrEP discontinuation (Table 5). At their last study visit, 31% (93/298) of participants reported currently taking PrEP.

DISCUSSION

In this study of 298 YBMSM in Atlanta, Georgia, provision of free PrEP clinical services and access to low- or no-cost medication led 44% to initiate PrEP, an increase from only 6% on PrEP at baseline. However, of those who initiated, more than two-thirds (69%) had at least 1 discontinuation. Although many who discontinued PrEP eventually restarted, more than half discontinued a second time, and 40% did not restart PrEP while under observation. Participants faced significant socioeconomic and

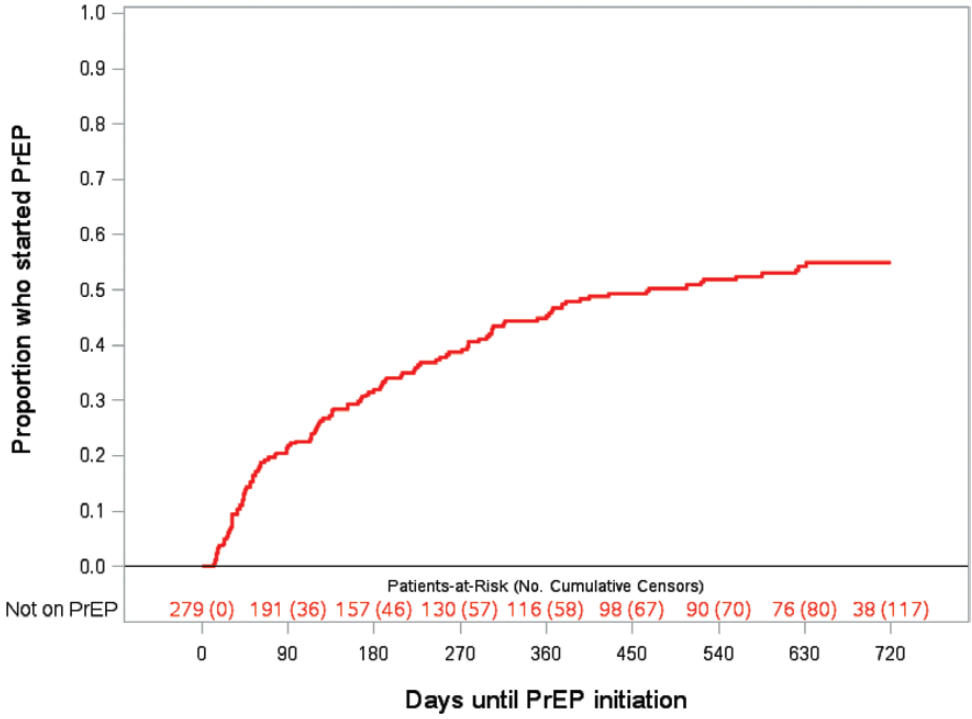

Figure 2. Cumulative incidence plot of time to first dose of PrEP (PrEP uptake). Participants taking PrEP at baseline (n = 19) are excluded from this plot. Abbreviation: PrEP, pre-exposure prophylaxis.

psychological challenges; the high rates of housing instability and mental health symptoms could contribute to PrEP discontinuation. Although public health efforts are appropriately focused on increasing access to PrEP, we showed that discontinuation was common among YBMSM, even with intensive PrEP navigation services. Simply providing access alone may not translate to the reduced HIV incidence seen among PrEP users in this study.

We had hoped for higher levels of PrEP uptake considering the high incidence of HIV and that more than 75% of participants

Table 3. Bivariate and Multivariable Cox Proportional Hazard Model for Pre-exposure Prophylaxis Uptake Among Young Black Men Who Have Sex With Men

Variable	HR	95% CI		*P* Value	AHR	95% CI		*P* Value
Age, y								
18–21	0.56	.33	.95	.03	0.64	.35	1.16	.13
22–25	0.83	0.57	1.22	.35	0.73	.48	1.13	.16
26–29	Ref	…	…	…	Ref	…	…	…
More than high school education	1.28	0.84	1.94	.25	1.29	0.80	2.09	.30
Income ≥$20 000 annually	1.20	0.84	1.71	.33	1.05	.71	1.56	.81
Health insurance	0.94	.66	1.35	.74	0.96	.64	1.44	.84
Depression symptoms[a]	0.89	.56	1.43	.63	1.09	.66	1.81	.73
High self-efficacy[b]	1.83	1.13	2.96	.01	2.03	1.23	3.34	.01
Cannabis use	0.72	.50	1.03	.07	0.71	.47	1.07	.10
Stimulant use	1.12	.72	1.74	.60	1.28	.79	2.06	.31
Risky alcohol use[c]	1.01	.69	1.50	.95	1.00	.65	1.55	1.00
Sexually transmitted infection in the past 12 months	1.80	1.27	2.57	<.01	1.67	1.15	2.44	.01
≤2 anal sex partners in the past 6 months	0.65	.45	.93	.02	0.72	.49	1.07	.10
Condomless anal sex in the past 6 months	1.86	1.16	2.97	.01	1.75	1.04	2.94	.04

Abbreviations: AHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio.

[a]Moderate to severe symptoms by patient health questionnaire-8 scale.

[b]Answered "exactly true" to "I can always manage to solve difficult problems if I try hard enough."

[c] Alcohol Use Disorders Identification Test.

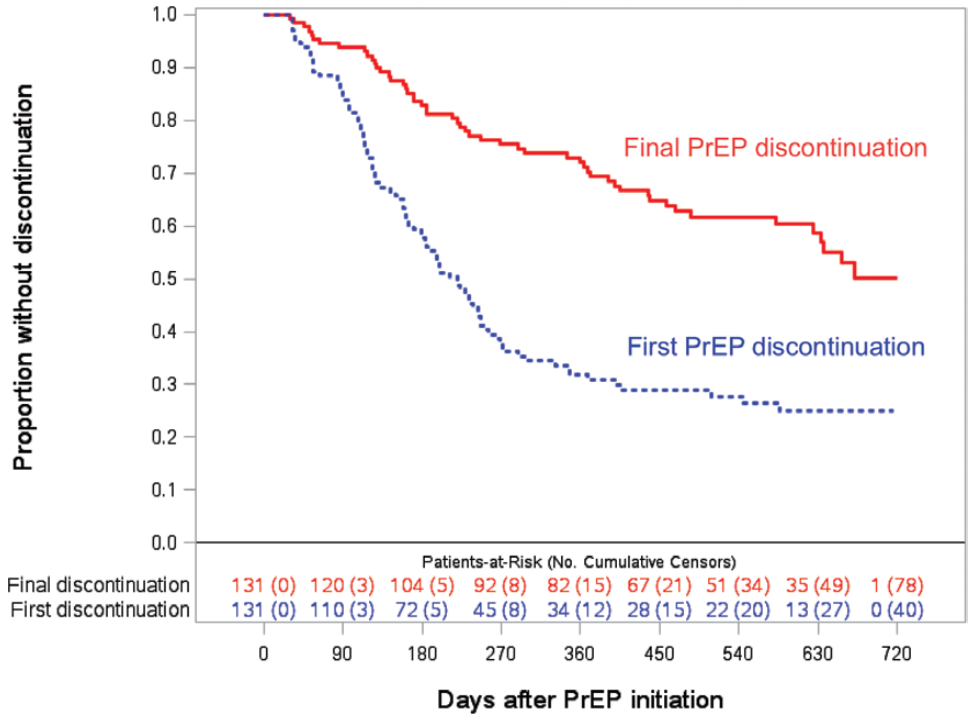

Figure 3. Kaplan-Meier survival plot of time to first and final pre-exposure prophylaxis discontinuation. Abbreviation: PrEP, pre-exposure prophylaxis.

reported CAI. In a qualitative study in this cohort, participants reported low perceived HIV risk and high confidence in their ability to use condoms as reasons not to use PrEP [14]. Uptake was slow, with some participants deciding to start PrEP more than 18 months into the study after being offered PrEP at multiple study visits, indicating a need for recurrent offers in this population. Individuals' reasons for slow PrEP uptake were not directly ascertained, and this is an area in need of further study. In-depth interviews were conducted and will be analyzed qualitatively in future work. The strongest predictor of PrEP uptake was having high self-efficacy for problem-solving as has been reported in another PrEP cohort [18]. Interventions using PrEP navigation and motivational interviewing to improve self-efficacy show promising results to increase PrEP uptake [27, 28].

Table 4. Bivariate and Multivariable Cox Proportional Hazard Model for First Pre-Exposure Prophylaxis Discontinuation Among Young Black Men Who Have Sex With Men

Variable	HR	95% CI		*P* Value	AHR	95% CI		*P* Value
Age, y								
18–21	4.37	2.40	7.95	<.01	4.34	2.21	8.52	<.01
22–25	1.65	1.03	2.63	.04	1.16	.69	1.96	.57
26–29	Ref	…	…	…	Ref	…	…	…
More than high school education	0.67	.42	1.08	.10	0.64	.38	1.09	.10
Income ≥$20 000 annually	0.88	.58	1.34	.55	1.22	.76	1.98	.41
Health insurance	0.75	.49	1.13	.17	0.67	.43	1.06	.09
Depression symptoms[a]	1.09	.63	1.91	.75	1.44	.73	2.86	.30
High self-efficacy[b]	1.28	.69	2.34	.43	0.77	.39	1.49	.43
Cannabis use	1.72	1.1	2.68	.02	1.77	1.03	3.06	.04
Stimulant use	1.47	.91	2.37	.12	1.52	.85	2.71	.16
Risky alcohol use[c]	0.73	.46	1.15	.17	0.82	.47	1.43	.48
Sexually transmitted infection in the past 12 months	1.18	.78	1.79	.42	1.78	1.09	2.88	.02
≤2 anal sex partners in the past 6 months	1.98	1.30	3.03	<.01	2.31	1.44	3.70	<.01
Condomless anal sex in the past 6 months	0.63	.37	1.06	.08	0.90	.49	1.67	.75

Abbreviations: AHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio.

[a]Moderate to severe symptoms by patient health questionnaire-8 scale.

[b]Answered "exactly true" to "I can always manage to solve difficult problems if I try hard enough."

[c] Alcohol Use Disorders Identification Test.

Table 5. Bivariate and Multivariable Cox Proportional Hazard Model for Final Pre-exposure Prophylaxis Discontinuation Among Young Black Men Who Have Sex With Men

Variable	HR	95% CI		*P* Value	AHR	95% CI		*P* Value
Age, y								
18–21	4.53	2.09	9.81	<.01	3.83	1.61	9.12	<.01
22–25	1.89	.97	3.68	.06	1.31	0.62	2.75	.49
26–29	Ref	…	…	…	Ref	…	…	…
More than high school education	0.97	.50	1.89	.93	0.92	.43	1.99	.83
Income ≥$20 000 annually	1.10	.63	1.92	.73	1.83	.91	3.68	.09
Health insurance	0.97	.56	1.68	.92	1.00	.54	1.87	1.00
Depression symptoms[a]	1.40	.72	2.73	.32	1.30	.57	2.93	.53
High self-efficacy[b]	1.30	.59	2.89	.51	1.07	.43	2.67	.89
Cannabis use	1.74	.96	3.15	.07	2.12	1.01	4.45	.05
Stimulant use	2.28	1.27	4.10	<.01	2.01	.98	4.10	.06
Risky alcohol use[c]	0.67	.36	1.25	.21	0.65	.30	1.39	.27
Sexually transmitted infection in the past 12 months	0.91	.53	1.57	.73	1.08	.56	2.07	.83
≤2 anal sex partners in the past 6 months	1.98	1.12	3.51	.02	2.36	1.22	4.57	.01
Condomless anal sex in the past 6 months	0.67	.34	1.35	.26	0.79	.35	1.77	.56

Abbreviations: AHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio.

[a]Moderate to severe symptoms by patient health questionnaire-8 scale.

[b]Answered "exactly true" to "I can always manage to solve difficult problems if I try hard enough."

[c] Alcohol Use Disorders Identification Test.

Among those who initiated PrEP, we noted high rates of discontinuations over study follow-up. Our results are consistent with national pharmacy data showing 44% discontinuation at 1 year after PrEP initiation, with younger age being associated with discontinuation [12]. Based on the low positive predictive value (PPV) of self-reported adherence for protective levels of TFV-DP in DBS samples, our results are likely an overestimate of PrEP persistence and represent a "best-case scenario" in this cohort. We presume that there were multiple other unrecorded shorter periods of discontinuation within our liberal estimates of persistence. Alternatively, participants may have been using PrEP on-demand or less than daily, leading to fewer refills and less follow-up, although only daily PrEP was endorsed by the study. The repeated contact with study staff and ongoing counseling likely led to more PrEP reinitiations than would be expected in usual practice.

It is possible that some PrEP discontinuations in our cohort were medically indicated. For example, we found more discontinuation among those with fewer anal sex partners. However, the high incidence of HIV seen in both PrEP users and nonusers in our cohort supports persistence on therapy as important for this specific population, particularly given the high prevalence of HIV in sexual networks of YBMSM in the South [29]. Furthermore, others have shown that HIV incidence remains substantial even in those who discontinue PrEP for reasons that are considered appropriate [30]. We agree with others who suggest that PrEP guideline indications should take into account different epidemiologic risk groups in defining indications for PrEP rather than exclusively focusing on past or current risk behaviors [31].

Although our cohort was entirely YBMSM aged 18–29 years, PrEP discontinuation was highest among the youngest men (aged 18–21 years). These data provide new and complementary real-world reinforcement of findings from adolescent/young adult PrEP clinical trials showing very low adherence in this population [32]. Younger YBMSM may have less access to healthcare and less experience navigating these complex systems [33]. Future research should focus on reasons for PrEP discontinuation among young MSM in order to develop interventions that support persistence. Specific research on multimodal HIV prevention packages in YBMSM are needed, and preliminary data show that even low-intensity mobile health interventions can have a significant impact on PrEP adherence [34, 35].

Substance use is common among YBMSM and is associated with sexual risk behaviors, STIs, and HIV incidence [36–38]. Our finding that cannabis use was independently associated with PrEP discontinuation has not been previously reported, and the high prevalence of cannabis use could have significant public health implications. The effect of cannabis use on PrEP discontinuation warrants further study. It is not clear if cannabis use directly caused PrEP discontinuation or if it is a marker for socioeconomic or psychological factors for which we could not statistically control. Heavier cannabis users accounted for most of the association, which points to potential causality. Similarly, a positive urine drug screen for stimulant use was also associated with discontinuation. Interventions aimed at treating substance use disorders and decreasing substance use have the potential to decrease HIV incidence both by decreasing drug use–associated risk behaviors and drug use–associated PrEP discontinuation.

STI diagnosis is the most direct surrogate for HIV risk, and it is especially concerning that STIs were associated with a 78% increase in the hazard of PrEP discontinuation, similar to findings by Hojilla and colleagues [39]. If STI diagnosis is a marker of less adherence to health promotion behaviors, such as condom use, then a similar rationale could explain why these participants were also more likely to discontinue PrEP. Because STI was strongly associated with PrEP uptake, participants may have higher levels of perceived HIV risk. Nonetheless, in our qualitative data, participants reported that STI diagnosis was a sign that they needed to "slow down," use condoms, and decrease their overall sexual activity, rather than a reason to use PrEP [14].

The use of primarily self-report of PrEP persistence was prone to recall bias and observer bias and did not necessarily indicate adherence, especially in the context of the low PPV of self-report for protective TDF levels. This study did not completely mimic usual clinical practice; PrEP services were provided for free, we had increased resources to support adherence, and participants continued follow-up with the EleMENt study even if they discontinued PrEP. Predictors of PrEP uptake/discontinuation were exploratory and do not necessarily indicate causal relationships. Finally, based on our sample size, statistical power was limited for some tested associations.

CONCLUSIONS

In a cohort of sexually active YBMSM in the southern United States with access to free PrEP services, PrEP discontinuations were common and multiple. While many who discontinued PrEP restarted at some point during study follow-up, this was not without significant gaps in PrEP coverage amidst high observed HIV incidence. Interventions aimed at promoting persistence among the youngest YBMSM and substance-using MSM are crucial to decreasing HIV incidence in this key population.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. D. P. S. performed data analyses and wrote the initial draft of the manuscript. P. S. S., C. F. K., E. S. R., and C. M. R. were involved in grant writing, study design, and study protocol. All authors assisted in the design of the analyses and interpretation of the results and provided substantial edits to the text of the manuscript.

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