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David Phillip Serota, MD Date

Approval Sheet

The Effects of Substance Use and Mood Disorders on the Use of HIV Pre-Exposure Prophylaxis Among Young Black Men Who Have Sex with Men

By

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Master of Science

Clinical Research

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Abstract Cover Page

The Effects of Substance Use and Mood Disorders on the Use of HIV Pre-Exposure Prophylaxis Among Young Black Men Who Have Sex with Men

By

David Phillip Serota
ScB, Brown University, 2009
MD, University of Miami Miller School of Medicine, 2013

Advisor: Colleen F. Kelley, MD, MPH

An abstract of a thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Master of Science in Clinical Research
2019

ABSTRACT

The Effects of Substance Use and Mood Disorders on the Use of HIV Pre-Exposure Prophylaxis Among Young Black Men Who Have Sex with Men
By David Phillip Serota

Background
Daily HIV pre-exposure prophylaxis (PrEP) is >95% effective in preventing HIV infection among populations at increased risk. Young black men who have sex with men (BMSM) in the southeast are the demographic with the highest HIV incidence in the United States, but have inadequate PrEP uptake and persistence on PrEP. The objective of this research was to investigate whether the high prevalence of substance use and mood disorders among young BMSM leads to inadequate PrEP.

Methods
The EleMENt cohort is a prospective observational cohort of HIV-negative young BMSM in the Atlanta. Participants are offered enrollment in an optional PrEP program, that provides clinical services for PrEP, prescriptions, and assistance paying for medication. The association between substance use and the prevalence of mood disorders was evaluated using logistic regression. Kaplan-Meier survival functions were created for time to PrEP initiation and time to PrEP discontinuation. Cox proportional hazards models were created to identify how substance use, mood disorders, and other covariates were associated with PrEP uptake and PrEP discontinuation.

Results
298 HIV-negative young BMSM were followed longitudinally for 24 months. There was a 30% prevalence of moderate to severe mood disorder symptoms at baseline. Sixty eight percent used marijuana, 14% used cocaine, and 30% had risky alcohol use. Forty two percent (125/298) initiated PrEP during the study period. Marijuana was associated with less PrEP uptake and higher education, self-efficacy, and STIs with more uptake. Of the 125 who initiated PrEP, 79 (63%) discontinued PrEP during follow up. Marijuana use was associated with more discontinuation along with younger age and fewer sex partners. Cocaine use, risky alcohol use, and mood disorders had no association with either PrEP uptake or discontinuation and there was no statistical interaction between substance use and mood disorders.

Conclusions
PrEP uptake and persistence in this cohort of young BMSM was suboptimal despite education and access to free PrEP services. Marijuana use was associated with both less PrEP uptake and more discontinuation, while the other substances and mood disorders had no significant effect. Special attention to the youngest and marijuana using BMSM is needed to maximize PrEP effectiveness in this key population.

Cover Page

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Lastly, I would like to thank my wife Zabrina Quidiello for her love, support, patience, and graphic design consultation.

This work is dedicated to my mother, Gail D. Serota, who gleefully read any piece of work I ever published and snuck into medical conferences around the globe to watch me present. She would have certainly read this tome from cover to cover.

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INTRODUCTION

Unacceptably high rates of HIV incidence continue to occur in the US, especially among certain populations such as young black men who have sex with men (YBMSM). In a previous study conducted by our group in Atlanta, GA, we noted an annual HIV incidence rate of 11% among young black MSM (1). In 2014, the Centers for Disease Control and Prevention (CDC) recommended routine use of pre-exposure prophylaxis (PrEP) to prevent HIV in people at high risk. Daily oral PrEP with tenofovir/emtrictiabine (TDF/FTC) use can result in >90% efficacy in preventing HIV acquisition. However, at-risk populations must have access to this expensive medical intervention, frequent healthcare contact, and persistence of medication use in order to achieve this level of efficacy. Identifying, understanding, and addressing barriers to achieving PrEP uptake and persistence in the highest risk populations are crucial to successful implementation. The use of PrEP remains low among young BMSM in Atlanta, GA; only 4.7% of MSM in Atlanta report using PrEP in the last 12 months (2). The EleMENt study is an ongoing prospective cohort study of HIV-negative YBMSM in Atlanta, GA designed to evaluate longitudinal relationships between substance use and HIV risk behavior. As part of this study, all participants are offered optional PrEP in addition to a standard package of HIV prevention services. In this cohort study, detailed demographic, HIV risk behavior, mental health symptoms, and substance use data are collected longitudinally on all participants. Therefore, this study gives the unique opportunity to evaluate factors associated with uptake and persistence of PrEP use in young BMSM in a setting ensuring education and access. Understanding the impact of these factors on PrEP awareness, attitudes, uptake, and persistence among young BMSM is critical to addressing its under-utilization and will form the basis of future interventions to improve PrEP uptake and persistence for this population. In this thesis,

I will identify and quantify factors that predict PrEP uptake and persistence in a high-risk underserved population with a specific focus on substance use and mood disorder symptoms.

BACKGROUND

Young black men who have sex with men (BMSM) in the southeast have the highest HIV incidence of any risk group in the United States. Men who have sex with men (MSM) continue to the be the most at-risk group for HIV infection in the United States; despite making up only 4% of the US population, MSM accounted for 68% of all new HIV infections from 2010-2015 (3). Atlanta, Georgia had the 4th highest rate of new HIV diagnoses of all US metropolitan areas in 2016; the rest of the top 9 were all located in the southeast as well (3). As in other large municipalities, African-American people are disproportionately affected by HIV; in Atlanta they comprise 69% of persons living with HIV while making up only 30% of the local population (4). The PRISM Health study group at the Rollins School of Public Health completed the InvolveMENt study in 2014 where we documented large racial disparities between black and white MSM in the prevalence of HIV at study initiation as well as incidence over the course of the study. Prevalence of HIV at baseline was 43% for black MSM compared to 13% for white MSM (5). The incidence of HIV was 11% per year among black MSM aged 18-25 versus only 1.7% per year among similarly aged white MSM (1). In that study, the primary explanatory variables for the disparity was lower rates of health insurance and more black partners among the black MSM versus white MSM. There is an urgent need for effective HIV prevention interventions to be deployed specifically among young BMSM in the southeast.

PrEP is effective at reducing HIV transmission and has potential to make a significant impact on the HIV epidemic. Efficacy of PrEP has been demonstrated to be greater than 90% when detectable study drug is present in blood samples of users (6, 7). PrEP is an expensive biomedical intervention; however it has been shown to be

cost effective especially when background HIV prevalence is high (~35%) (5, 8). This evidence led the Centers for Disease Control and Prevention (CDC) to recommend PrEP for all MSM at increased risk of HIV in 2014 (9). Studies through the National Health Service in the United Kingdom (10) and Kaiser Permanente in Northern California (11) also showed effectiveness of PrEP in a broader real-world population of MSM. However, black MSM only made up 10% of participants in the UK study. In the Kaiser study, only 4.3% of PrEP users were black, whereas black MSM previously made up 24% of HIV seroconversions in their health system (12).

The utility of PrEP as a public health intervention to reduce HIV incidence is directly proportional to the number of at-risk people using PrEP in addition to the length of therapy (i.e. PrEP persistence). Over ten years, population coverage of 40% of HIV-negative MSM with PrEP is estimated to prevent 25% of new HIV infections (13). If coverage can reach 80%, PrEP would prevent approximately 40% of new HIV infections. Based on PrEP usage data from 2016, it is estimated that PrEP decreased the incidence of HIV by 18.1% (14). PrEP implementation is far from optimal at this time. We have previously proposed a PrEP care continuum, analogous to the HIV care continuum, to identify barriers to widespread coverage of PrEP in Atlanta MSM (15). In 2014, only 4.7% of MSM in Atlanta reported taking PrEP in the last 12 months (2). From 2012 to 2016 the rates of PrEP usage increased, but has since plateaued (16).

Disparities in PrEP uptake between risk groups have emerged and could exacerbate disparities in HIV prevalence. Nationally, black MSM were half as likely to have taken PrEP in the last year than white MSM (2). Despite the higher rate of HIV incidence in black MSM, they were also less likely to meet CDC guideline indications for PrEP. This is consistent with prior studies that demonstrate current risk assessment tools, that generally rely on self-reported risk behavior, do not accurately predict HIV

risk among black MSM (17, 18). BMSM make up 44% of new HIV infections, but they only accounted for 10% of people taking PrEP in 2016 (16). BMSM have the highest need for PrEP based on CDC indications (though the guidelines seem to underestimate the risk), and based on those indications, only 1% of eligible BMSM are taking PrEP (19, 20). Therefore, it is of critical importance to identify barriers to PrEP uptake and persistence in young BMSM in order to reduce HIV incidence in this population. If PrEP is not implemented in a more equitable manner, it is likely to widen the gap in HIV incidence between black and white MSM in the United States (21).

Thus far, there has been poor adherence and retention in PrEP care, both of which have been more likely for black MSM. Beyond PrEP knowledge, willingness, access, and uptake, there remain difficulties maintaining people on PrEP over time (PrEP persistence). In a cohort of insured MSM in northern California, 12.9% of PrEP users were non-adherent (<80% doses taken) and 22.5% discontinued PrEP over a 3 year period, with black patients being more likely to be non-adherent (RR 3, 95% confidence interval 1.7 to 5.1) (22). In young MSM in Chicago, 33% of study participants who initiated PrEP at some time had discontinued at the time of interview with discontinuation being more likely among black and Hispanic participants. Similar findings of lower adherence among black MSM was seen in a PrEP demonstration project in Miami, Washington, DC, and San Francisco (23). Most striking are findings of the Adolescent Trials Network 110 PrEP demonstration project, where young MSM provided PrEP were only 34% likely to have therapeutic drug levels at week 48 of the study (24). It is crucial that we gain a better understanding of barriers and facilitators of PrEP uptake and persistence in young BMSM.

Substance use is prevalent among MSM and is associated with high-risk sexual behaviors. In the United States, those between the ages of 18 and 25 have the highest rates of heavy alcohol use, binge drinking, illicit drug use, and substance use disorder diagnoses (25). Illicit substance use is more common in MSM compared to the general population with 40% of MSM reporting illicit substance use in the last month (26) compared to 10.1% of the general US population (25). Associations have been reported between condomless anal intercourse (CAI) and use of amphetamines, cocaine, alcohol, marijuana, amyl nitrites (poppers), ecstasy, and "alcohol or drugs" (more broadly defined) (27-34). Using drugs to facilitate sex or increase pleasure has been increasing in the United Kingdom, predominantly with the use of stimulants (mephedrone, amphetamine) and gamma-hydroxybutryic acid (GHB) (35, 36). Drug use for sex is associated with increased risk behaviors as well as increased HIV incidence (adjusted OR 5.06; 95% CI 2.56 to 10.02) (37). In the InolvMENt study we also found that among young BMSM, self-report of substance use was an insensitive measure compared to biomarker-proven substance use with urine drug screening results (38).

Symptoms of mood disorders are prevalent among MSM and are associated with high-risk sexual behaviors. Lesbian, gay, and bisexual populations have approximately double the lifetime risk of developing a mood disorder (anxiety or depression) compared to heterosexuals (39). This has been attributed to the "minority stress" concept, where sexual minorities experience high rates of stigma, prejudice, and discrimination, which contribute to development of psychopathology. The HIV Prevention Trials Network 061 study (HPTN 061) showed a baseline prevalence of depressive symptoms of 43.8% among black MSM primarily between the ages of 18 and 47 (40). There have been mixed results associating mood disorder symptoms with risky sexual behaviors and HIV/STI incidence/acquisition (41-44); however, specifically

among black MSM, the association has been more definitive (45). Among black MSM in Boston (mean age 38.5 years old) those with moderate depressive symptoms were more likely to report CAI with a serodiscordant partner (OR 9.86) than those with low depression symptom scores. To date, there has been little evaluation of the effect of anxiety symptoms, isolated from depression, on sexual risk behaviors and HIV acquisition.

Substance use and symptoms of anxiety and depression may have an impact on PrEP uptake and persistence. It is important to evaluate how substance use and mental health disorders impact PrEP uptake and persistence in young BMSM as it will better inform our ability to implement this powerful tool in this key population. The effects of substance use and mental health disorders on real-world PrEP uptake and persistence have been understudied to date. Most research in this area has been qualitative; evaluating research participants' intention to use PrEP or reasoning for non-adherence and discontinuation. Little is known about "hard outcomes" or PrEP uptake and persistence with relation to substance use and mood disorders.

Oldenburg et al explored attitudes toward PrEP in non-IV drug using MSM, specifically comparing between those with alcohol use versus stimulant use (46). They found that stimulant users worried about adherence to PrEP whereas those with alcohol use were more concerned about stigma of taking PrEP. They used self-report substance use only, which was an insensitive measure in our prior studies, and did not explore other substances or compare to non-substance users. The same group also studied PrEP attitudes in MSM with alcohol or stimulant use disorder comparing between those with and without "transactional sex" (47). The main finding was that those with transactional sex were more likely to worry about stigma of being on PrEP. Both of these studies included few black participants and recruited subjects from the Northeastern US. In our

study, we will assess the relationship between substance use and mood disorder symptoms on PrEP uptake and adherence exclusively in young BMSM. Also, these studies' main outcome was "PrEP attitudes" whereas our study will focus on more clinically important outcomes.

One of the few studies of depression and PrEP outcomes, a post-hoc analyses of the iPrEX study, showed that depressive symptoms did not have an association with blood levels of TDF/FTC (surrogate for adherence) (48). Because this was a highly protocolized randomized controlled trial, it was not able to explore how depression affects uptake of PrEP prior to study entry. In the iPrEX open label extension study, participants who reported stimulant use were more likely to be non-adherent to PrEP, but had no difference in HIV incidence between those who did not use drugs (49). There is urgent need to understand factors predicting PrEP uptake and persistence in this key population so that this effective intervention can be best implemented to reduce HIV incidence.

Qualitative studies have shown that substance using MSM underestimate their HIV risk, which could be one pathway leading to worse PrEP outcomes (50). At the same time, we know that having more partners and more unprotected sex are associated with better PrEP retention and adherence. Because substance use is associated with more HIV risk behaviors, but more HIV risk behaviors are associated with better PrEP outcomes, the relationship between substance use, sexual risk, and PrEP remains nebulous.

METHODS

Aims: This is a prespecified secondary analysis of a prospective longitudinal cohort study of HIV-negative young black men who have sex with men in Atlanta, Georgia.

Aim 1: To examine the association between substance use and mood disorders, specifically, anxiety and depression, among HIV-negative young BMSM.

Aim 2: To evaluate the effects of substance use and mood disorders on PrEP uptake in a cohort of young black men who have sex with men.

Aim 3: To evaluate the effects of substance use and mood disorders on PrEP discontinuation in a cohort of young black men who have sex with men.

Study overview and population: The EleMENt study is a prospective cohort of 300 BMSM in Atlanta, Georgia, aged 18-29 years, established to understand the pathways by which substances influence HIV/STI risk. A detailed description of study design has been published elsewhere (51). Enrollment was completed in June 2015 with follow-up continuing through 2019. Participants include HIV-negative young BMSM who reported ≥1 male sexual partner in the 3 months prior to enrollment. Participants were recruited using venue-based time-space sampling (VTS) and Internet recruitment (e.g. Facebook, dating sites) in the Atlanta metropolitan area (52). Potential participants were not asked about HIV status prior to the baseline study visit.

Baseline data was collected on all enrollees and HIV-negative participants were followed longitudinally. Overall 469 participants were enrolled, 169 of whom were not included in these analyses, to establish a cohort of 300 HIV-negative participants. HIV-negative men were followed longitudinally with study visits at 0, 3, 6, 18, and 24 months. At visits, participants were tested for HIV using a rapid test, syphilis, and urethral and rectal chlamydia and gonorrhea. Rapid test HIV-negative participants received

qualitative HIV nucleic-acid amplification testing, as part of an acute HIV-infection detection protocol (53). All participants received comprehensive HIV/STI risk-reduction counseling which included the provision of condoms and lubricants. Substance use biomarker collection consisted of a self-contained, one-step, 7-drug panel test (iCup Drug Test Cup, BioScan Screening Systems), to detect, with varying windows of detection, marijuana (up to 30 days), cocaine (4 days), opioids (4 days), amphetamines (4 days), ecstasy (3 days), methamphetamine (5 days), and phencyclidine (PCP, 14 days). Participants completed a computer-assisted self-interview (CASI) questionnaire to assess demographics, substance use patterns, mental health symptoms, HIV prevention behaviors, including previous PrEP awareness and use, and HIV sexual risk factors. The study protocol was reviewed and approved by the institutional review board of Emory University.

Optional PrEP program: Based on previous observations of high HIV incidence among young BMSM in Atlanta (1) and the ethical obligation to ensure access to the most effective HIV prevention modalities, we offered non-incentivized PrEP as standard of care to all HIV-negative participants (51). All participants were educated about PrEP at study visits and were offered the opportunity to meet with a study physician for PrEP initiation. All men who expressed interest in PrEP were scheduled for a separate visit with a study physician. PrEP initiation visits consisted of consultation with a physician for further education, medical evaluation for appropriateness, screening for symptoms of acute HIV infection, and adherence and risk-reduction counseling.

Tenofovir-emtricitabine (TDF/FTC) was not directly provided through the study, but a patient navigator assisted with free or low-cost medication access via the participants' health insurance plan and/or the manufacturer assistance programs. Laboratory testing including evaluation for hepatitis B, renal function, and STI testing

was completed according to Centers for Disease Control and Prevention guidelines (54). To offer PrEP directly within the cohort without the need for referral or navigation to external PrEP services, we obtained supplemental funding for financial coverage of provider visits and laboratory costs. At follow-up study visits, participants in the PrEP program completed an additional PrEP survey that included assessment of adherence, reasons for missed doses, dosing strategies (if participants have used PrEP on-demand), sharing of medication, and thoughts about stigma, satisfaction, and how PrEP might be affecting sexual risk behaviors.

Data sources: All exposure variables were collected from the baseline study visit survey and laboratory testing with the exception of food security (see below). All self-report data was collected using a computer assisted survey instrument that could be completed at the study visit or remotely through a secure linked online survey. Laboratory results were entered by research assistants. PrEP uptake information was collected by the PrEP coordinator from a 1 month phone call with participants who had attended a PrEP initiation visit.

For each participant who attended a PrEP initiation visit, we created a timeline of PrEP use during the study follow up. At each point of contact, we assessed whether the participant was taking PrEP (defined as self-report of ≥4 doses/week) or not. Time points included dates of study visits where adherence was assessed, telephone and e-mail contact with study staff, and dates of prescriptions and patient assistance program expiration.

Variable definitions:

Sociodemographics: Age was used both as a continuous variable and dichotomous between those ≥22 years and those <22 years old. This cutoff was chosen based on

literature identifying particularly low PrEP uptake and persistence among adolescent and the youngest young adults (24, 55). Education and income were both dichotomized to "high school or greater education" and annual income ≥$15,000, respectively. Food insecurity was defined as low or very low food security based on the U.S. Household Food Security Survey Module: Six-Item Short Form. These questions were only performed at the month 3 visit, so some participants skipped this visit or had not yet completed the visit at the time data was pulled.

Mental health: To assess depressive symptoms, all participants completed the PHQ-4 survey. If they scored 2 or greater on either of the first two items, they then completed the full PHQ-8 (56). Cut-offs of 5, 10, and 15 points were used to establish mild, moderate, and severe symptoms of depression, respectively. Participants completed the GAD-7 to assess for symptoms of anxiety. For GAD-7, scores of 5, 10, and 15 are taken as the cut-off points for mild, moderate and severe anxiety, respectively (57). Both scales were used in a dichotomous fashion between "moderate or severe symptoms" vs "none or mild symptoms". Because there is a high prevalence of co-occurring anxiety and depression among young adults, we used a composite of "moderate to severe anxiety *or* depressive symptoms" as the exposure of interest. Participants were also asked if they have received a diagnosis of anxiety or depression from a physician or mental health provider and whether they are receiving treatment (pharmacotherapy or behavioral interventions).

Substance use: The survey included detailed questions about substances used, frequency, reasons for use, and circumstances of use. The Alcohol Use Disorders Identification Test (AUDIT) was used to assess alcohol consumption. A cutoff of ≥8 was used as a positive screen for "risky alcohol use". Presence of baseline substance use was established by

creating a copositive variable of self-report (used substance within the past 6 months) or urine drug screen positivity.

Sexual behavior: Presence of STI was a composite variable, defined as positive baseline testing for gonorrhea, chlamydia, or syphilis or self-report of any STI in the preceding 12 months. Condomless anal intercourse (CAI) was defined as self-report of ≥1 anal or oral sex partner without condom use in the preceding 6 months.

PrEP uptake and discontinuation: 'PrEP uptake' was defined as a participant attending a PrEP initiation visit and then at a 1-month follow up phone call confirming that they had filled their prescription and started taking TDF/FTC. Each participant estimated the date that they took their first dose, which defined the day of the event. A subset of those who attended a PrEP initiation physician visit never ended up taking medication; these participants were not included in the 'PrEP uptake' group. Time to PrEP initiation was recorded. If someone never initiated PrEP, they were censored at the time of their 24 months visit. Because this was an interim analysis, those who had not completed the study were censored at the time the uptake data was pulled in July 2, 2018.

In the PrEP discontinuation analyses, the denominator was all participants who had 'PrEP uptake' at any time during the study. In those participants 'PrEP discontinuation' was defined as having a ≥14 day period off PrEP after the date of PrEP initiation (uptake). Thus, the outcome of PrEP discontinuation was defined at time to first PrEP discontinuation. If a participant who began PrEP never had a discontinuation, they were censored at the time of their month 24 visit or the date of interim data acquisition (August 15, 2018). Different interim dates were used for the PrEP uptake and discontinuation models.

Determination of PrEP discontinuation was achieved using multiple sources of data including: participant self-report at each study visit, telephone call log with participants, pharmacy refill records (when available), prescription dispensation dates, and expiration dates of drug manufacturer assistance programs. Using this data, a timeline was manually created for each PrEP initiator with time blocks defined by any available information from the listed data sources and then a judgement was made of whether the participant was on or off PrEP during that period. If a data source identified someone as being off PrEP, the date of discontinuation used was taken to be halfway between the last known date on PrEP and the date when they were identified as being off PrEP.

Statistical analyses by aim:

Descriptive statistics: Baseline sociodemographic, substance use, mental health, and sexual behavior information were obtained for the entire cohort. Categorical variables are presented as percentages and continuous variables as medians with interquartile range (IQR). The amount of missing data for each variable is also presented.

Aim 1: To examine the association between substance use and mood disorders, specifically, anxiety and depression, among HIV-negative young BMSM.

There is a bidirectional causal relationship between substance use and mood disorders. For example, severe depression can predispose to substance use; but similarly, heavy substance use can lead to substance induced mood disorders. Because substance use is the primary exposure of interest for aims 2 and 3 as well as the larger EleMENt study overall, aim 1 used substance use as the independent variable and mood disorders as dependent variable, by convention. The goal of this aim was to document how substance use impacts mood disorders in young BMSM, with particular interest in how

different substance and different levels of exposure are associated with mood disorders. The association between substance use and active mood disorder symptoms (by PHQ-8 and GAD-7) was the primary objective. We also analyzed this data including report of a diagnosed mood disorder with or without active symptoms.

Data for this aim was all taken from the baseline survey. Because this was a cross-sectional analysis and because the outcome (mood disorder symptoms) had a prevalence >10%, we used prevalence ratios (PR) rather than odds ratios to describe the relationships. Bivariable analyses were performed relating different substances and doses with the prevalence of mood disorder symptoms. P-values for the chi-square test and fisher exact test (when ≥25% of expected values were <5) are provided. For variables with enough data, the associations were adjusted for demographic variables that could confound the relationship between substance use and mood disorders: age, income, insurance, and education. Because this aim was primarily an exploratory analysis to inform the modeling and interpretation of aims 2 and 3, there was no correction for multiple comparisons.

Aim 2: To evaluate the effects of substance use and mood disorders on PrEP uptake in a cohort of young black men who have sex with men.

The main exposures of aims 2 and 3 were mood disorder symptoms, marijuana use, cocaine use, and risky alcohol use. The outcome of interest for aim 2 was "time to PrEP uptake." Negative log-log survival functions were evaluated between the different levels of each categorical variable and the outcome of PrEP uptake. There were no gross violations of the proportional hazard assumption. Bivariable associations between variables and PrEP uptake were computed using a cox proportional hazards model. Next, multivariable cox proportional hazard models were used to examine the effect of each exposure of interest on PrEP uptake. A separate model was constructed to isolate the

effect of each exposure on the outcome (model 1: mood disorder, model 2: marijuana and cocaine use, model 3: alcohol use), then all exposures of interest were included in one model (model 4). Marijuana and cocaine use were examined in the same model to limit the number of models and because there is a known association between marijuana use and other drug use. Thus, we wanted to try to isolate the effect of each of these substances in the same model. Based on prior literature and hypothesized causal relationships, all multivariable models were adjusted for age, education level, insurance status, housing instability, self-efficacy for problem solving, STIs, and number of sexual partners in the last 6 months.

For model 4, which included all exposures of interest, we assessed for interaction between substance use and mood disorder symptoms. Based on the known association between substance use and mood disorders—and further explored in aim 1—we tested whether or not the effect of substances on PrEP use depended on whether or not a participant had mood disorder symptoms. A chunk test was performed with the product terms of mood disorders with each: marijuana use, cocaine use, and risky alcohol use. A P-value threshold of 0.05 was used as the decision threshold for the likelihood ratio test comparing the full (including interaction terms) and reduced (without interaction terms) models.

<u>Aim 3: To evaluate the effects of substance use and mood disorders on PrEP discontinuation in a cohort of young black men who have sex with men.</u>

The procedure for aim 3 was identical to that of aim 2, except that instead of the outcome being PrEP uptake, the outcome was time to first PrEP discontinuation.

Bias: Besides assessment of PrEP discontinuation, all survey data was collected anonymously by computer survey. We have previously described high rates of

underreporting of drug use among BMSM, so objective biomarker data was incorporated into the definitions of substance use (38). Similarly, due to possible underreporting of STIs, we included objective measures of STI (incident diagnosis) into this measure.

Missing data: There were 7 participants with minimal completion of their baseline survey. The most frequently missed question was about annual income. This was not included in the multivariable modeling of aims 2 and 3. For incomplete scales (PHQ-8, GAD-7, AUDIT), if a participant answered at least one question, the mean score of answered questions was scaled up to create an adjusted total score. Otherwise, complete case analysis was used for all analyses.

Sensitivity analyses: Prior analysis of these data (not published) identified a strong association between marijuana use and tobacco use. We hypothesized that the inclusion of tobacco in the multivariable models for aims 2 and 3 could hide any association of marijuana use with the outcomes of interest (covariance). As a sensitivity analysis, we repeated the multivariable models from aims 2 and 3 but including tobacco use.

Although there is a large overlap in the prevalence of anxiety and depressive symptoms, including in this study, it is possible that these symptoms could have differential effects on PrEP use. Thus, although the primary mental health exposure for this project was 'moderate-severe anxiety *or* depression symptoms,' we repeated the analyses including only depression symptoms and then again including only anxiety symptoms. Based on which mood disorder seemed to have a larger effect size, only one was included in the multivariable model.

The primary outcome of aim 3 was time to a *first* PrEP discontinuation. Many participants who had a PrEP discontinuation ended up restarting PrEP during the study. We created another outcome called 'Final discontinuation' which was defined as

someone stopping PrEP and never restarting before the study ended or the time of data acquisition (whichever came first).

To assess the validity of self-report of PrEP use, dried blood spot testing for tenofovir diphosphate (TFV-DF) levels was obtained for a subset of participants. Self-report of taking PrEP was compared against detection of any TFV-DF as well as against therapeutic TDF levels (>719 fmol/punch) (6).

Approval and Funding: The EleMENt study is approved by the Emory University institutional review board. The EleMENt study is funded through a grant from the National Institute on Drug Abuse (NIDA). The PrEP program is funded by a supplement from the Emory Center for AIDS Research (CFAR) and Gilead Sciences (Foster City, CA). David Serota received a TL-1 grant through the Georgia Clinical and Translational Science Alliance (CTSA) to complete this work. An earlier version of this work was presented by Dr. Serota at the 2018 Georgia Clinical and Translational Science Conference in Braselton, GA. Statistical analyses were conducted using SAS version 9.4 (Cary, NC).

RESULTS

Cohort characteristics

The EleMENt study enrolled 300 participants through June 2017 with follow up through February 2019. One participant was diagnosed with acute HIV infection at his baseline visit and was not followed longitudinally. One participant was doubly enrolled in the study; thus, the final longitudinal cohort was 298 participants. **Table 1** presents the baseline characteristics of the EleMENt cohort as well as the amount of missing data be variable. In keeping with the inclusion criteria for the study, median age was 24 (IQR 22-27) years old. One quarter had not completed high school and 31% earned less than $15,000 annually. More than half of the participants reported worry about housing and 9% had been homeless in the last 6 months before enrollment.

Mood disorder symptoms were common, with 20% reporting moderate to severe symptoms of depression, 23% with symptoms of anxiety, and 30% with either anxiety or depression symptoms. Fewer participants reported having received a diagnosis of anxiety or depression by a health care professional. There were 56 participants with mood disorder symptoms but no diagnosis of a mood disorder (**Supplementary Table 1**). Of those with diagnoses of mood disorders, more than half still screened positive for moderate-severe symptoms (30/55). Thirty-seven participants had both anxiety and depression symptoms, depression alone in 19, and anxiety alone in 29 (**Supplementary Table 2**).

Marijuana use was present in more than 2/3 of the cohort and cocaine in 14%. Other illicit drug use was infrequent. Risky alcohol use was present in 30% but higher levels—moderate to severe alcohol use disorder—were infrequent (data not presented). Tobacco use was present in 21% and diagnoses of hypertension in 10%. Sexually

transmitted infections in the prior year or at baseline visit were present in 42% and 77% reported condomless anal sex in the past 6 months.

Association between substance use and mood disorder symptoms

The relationship between substance use and mood disorders is explored in **Table 2** and **Table 3**. The prevalence of mood disorder symptoms was higher in participants who reported marijuana (PR 1.50, 95% CI 0.98-2.30, P=.05) or MDMA use (PR 1.88, 95% CI 1.18-3.00, P=.02). A similar pattern was seen for the prevalence of the composite of mood disorder symptoms *or* diagnosis. There was an association with higher grades of marijuana use (weekly and daily use) with mood disorder symptoms and diagnoses. The prevalence of many of the illicit substances was too low to draw conclusions, but the general direction of the association of substance use being associated with higher rates of mood disorders. There was no consistent relationship between measures of alcohol use and the prevalence of mood disorders. Multivariable models adjusted for potential demographic confounders are presented in **Table 3**. When alcohol was used specifically with the purpose of forgetting about one's problems, there was a statistically significant association with mood disorder symptoms (adjusted PR 2.01, 95% CI 1.39-2.89, P=.0002). Other variables associated with mood disorder symptoms included unemployment, housing instability (both 'housing worry' and homelessness), experience of discrimination, and a history of unfair treatment by police. Lower problem-solving self-efficacy was associated with mood disorders as well, though P >.05 in the adjusted models.

Effect of substance use and mood disorders on PrEP uptake

At the time of interim analysis, 154/298 (52%) of participants had reported interest in starting PrEP and had attended a PrEP initiation visit. A total of 125/298

(42%) had actually initiated PrEP, as measured by reporting a date when they took a first pill. Of the 29 participants who attended a PrEP initiation visit but never took a dose of medication, some had changed their mind about PrEP and others had encountered difficulties in obtaining the medication. A more detailed analysis of these cases has been published previously (51, 58). **Figure 1** shows a cumulative incidence function curve for time to PrEP uptake, with a time to 25th percentile uptake of 152 days (95% CI 113-210).

Bivariable associations between exposures of interest and time to PrEP uptake are displayed in **Table 4**. Older age, higher education level, STI history, and report of condomless sex were all associated with increased hazards of PrEP uptake after study enrollment. The strongest predictor of PrEP uptake was reporting high self-efficacy for problem solving (hazard ratio [HR] 2.01, 95% CI 1.22-3.32, P=.007). Marijuana and tobacco use were associated with less PrEP uptake. **Table 5** shows the multivariable models constructed to identify the effect of each individual exposure on PrEP uptake. Models 1, 2, and 3 show the adjusted HR (aHR) for each exposure of interest after controlling for the prespecified covariates: age, education, housing stability, insurance, self-effiacy, STI, and number of sex partners. Model 4 included all 4 exposures of interest. Notably, there is little difference in any of the parameters between the models. There was no effect identifiable for mood disorders, cocaine use, or alcohol use on the outcome of PrEP uptake. Marijuana remained significantly associated with less PrEP discontinuation in the adjusted models (aHR 0.63, 95% CI 0.42-0.94), P=.03. The likelihood ratio test for interaction had a P-value 0.12, indicating no interaction between substance use and mood disorders. Higher self-efficacy, STI diagnosis, and higher education remained significantly associated with PrEP uptake in the multivariable models.

Effect of substance use and mood disorders on PrEP discontinuation

Of the 125 participants who initiated PrEP at some time during the study, 79 (63%) had at least one PrEP discontinuation (≥14 days off PrEP after initiation). Of those who discontinued PrEP, 54 (68%) restarted PrEP, however the main outcome of these analyses is a 'first PrEP discontinuation'. **Figure 2** is a Kaplan-Meier survival curve of time to first PrEP discontinuation. After 219 days (95% CI 181-280), half of those who initiated PrEP, had discontinued.

Bivariable associations between the exposures and PrEP discontinuation (**Table 6**) show age <22 years (HR 3.55, 95% CI 2.05-6.15, P=.0001) and fewer than 3 sexual partners (HR 1.92, 95% CI 1.21-3.03, P.005) were strongly associated with PrEP discontinuation. No other variables were statistically significant in bivariable analysis. In the multivariable models (**Table 7**), marijuana (aHR 1.92, 95% CI 1.13-3.25, P=.01) was again the only exposure of interest with a significant association with the outcome; in this case, PrEP discontinuation. There was no interaction between substance use and mood disorder symptoms (Likelihood ration test P=.97)

Sensitivity analyses

PrEP uptake model: To evaluate whether the two mood disorders (anxiety and depression) might have differential effects on PrEP uptake, the models were run with each individual mood disorder (**Supplementary Table 3**). Neither anxiety nor depression individually had a statistically significant effect on PrEP uptake, however, comparing the two it seemed that anxiety had a larger magnitude of effect in the cohort (aHR 1.40 for anxiety versus 0.88 for depression). The p-values for anxiety and depression were 0.16 and 0.62 respectively.

The effect of tobacco use was evaluated by including this variable in the model. Even with tobacco included, the aHR for marijuana remained relatively unchanged and remained statistically significant. A more complete alternate model (Model 4 in

Supplementary Table 3) included anxiety alone as the mood disorder exposure as well as tobacco. In this model, the aHR for anxiety symptoms on PrEP uptake was 1.51 (95% CI 0.93-2.44, P= .09).

PrEP discontinuation model: A similar set of sensitivity models for PrEP discontinuation are presented in **Supplementary Table 4**. When investigating the differential effects of anxiety and depression for discontinuation, depressive symptoms had a larger effect, with aHR 1.79 (95% CI 0.88-3.65, P= .11). Tobacco use had no notable effect on the parameter for marijuana use. In a combined alternate model (Model 4 in **Supplementary Table 4**) the most notable change was that depressive symptoms had more indication of effect than when both mood disorders were combined.

Final PrEP discontinuation: At the time of these analyses, 39/125 (31%) of those who started PrEP had final discontinuation (median 690 days, 95% CI 581-∞). **Supplementary Figure 1** shows a Kaplan-Meier survival curve for time to final PrEP discontinuation. **Supplementary Table 5** shows a multivariable Cox proportional hazard model for final discontinuation. Age and marijuana use were the only variables associated with final discontinuation.

Biomarker validation of self-reported PrEP use: A subset of participants who initiated PrEP (n=65) had dried blood spot evaluation for levels of tenofovir diphosphate (TFV-DP), the active version of tenofovir. PrEP is considered efficacious at ≥4 doses per week, which correlates to the TFV-DP level of ≥719 fmol/punch (6, 59). **Supplementary Table 6** shows the comparison of TFV-DP levels with self-reported PrEP use at the same visit. Sensitivity of self-report was 0.93 and specificity 0.36.

DISCUSSION

While HIV pre-exposure prophylaxis has the potential to turn the tides of the HIV epidemic in the United States, thus far, its benefits have been limited (60) and inequitable across those at greatest risk (21, 61). In this prospective observational cohort of HIV-negative young black men who have sex with men in Atlanta, Georgia, compared to prior cohorts, we identified low uptake and high discontinuation of PrEP despite ensuring universal awareness and access to PrEP services. Prior work has identified population-level barriers to PrEP implementation among young BMSM (15, 58), whereas this study evaluated individual level factors impacting PrEP uptake and discontinuation. We demonstrated that marijuana use was the only variable associated with both less uptake and more discontinuation, while other substance use and mood disorders did not have a demonstrable impact on PrEP use. The psychosocial variables of education level and self-efficacy were associated with PrEP uptake along with history of STI. Of those who initiated PrEP, younger age and lower levels of reported sexual activity were most strongly associated with discontinuation. Understanding the causes of PrEP uptake and discontinuation is critical to improving PrEP implementation in this high incidence population.

Associations between substance use and mood disorders

We identified a consistent association between marijuana use and the prevalence of mood disorder symptoms with an approximately 50% increase in the prevalence of mood disorders among marijuana users versus non-users. This association held significant after controlling for demographics and various ways of quantifying marijuana use including urine drug testing, self-report, and frequency of use. With a baseline prevalence of mood disorder symptoms of 30% in the cohort, the aPR >1.5 is clinically

important from a public health standpoint because it represents a significant increase in the burden of mood disorders on a population level. While prior research has shown a strong association between “drug dependence” and associated depression and anxiety, this has been mostly focused on stimulants, such as methamphetamine (62). Prestage and colleagues performed a survey of mostly-white gay and bisexual Australians to investigate the association between substance use and mood disorders. They identified an association between marijuana use and depressive symptoms (OR 1.27, 95% CI 1.07-1.51, P=.008) in their cohort, which had similar rates of depression and substance use (62). There was no association between marijuana use and anxiety. A similar magnitude of association between marijuana and depression was seen in a survey of US adolescents (63), indicating a conserved association between these two variables across different populations.

There is biological plausibility that marijuana use could be directly causal of mood disorder symptoms. Although cross-sectional, in this analysis, mood disorders were defined by active symptoms at the time of survey, while the substance use implicitly preceded this temporally. Although not formally tested statistically, there was numeric progression in the aPR between marijuana and mood disorders with increasing frequency of use. Most striking from this study was the high prevalence of marijuana use (68%) with 15% (45/298) reporting daily use. The rate of cannabis use disorder among marijuana smokers is between 9% and 31% (64, 65), so there are likely to be a high number of participants with undiagnosed marijuana addiction, which can lead directly to symptoms of anxiety and depression.

It is difficult to draw conclusions about the effect of other drugs on mood disorder symptoms in this cohort due to low prevalence of use. In the study by Prestage and colleagues, the association of stimulant use with mood disorders was only apparent when restricting analyses to those with true stimulant use disorders. In our cohort,

stimulant use was relatively rare compared to rate reported among other MSM cohorts. Those who used, did so infrequently; thus, we did not have the power to detect a moderate association.

The prevalence of risky alcohol use was 30% and there was no clear signal of association with mood disorder symptoms. Although the level of risky use was high, the rate of true 'alcohol use disorder' was very low, as measured by the AUDIT and also by carbohydrate deficient transferrin levels. As with stimulant use, heavier levels of use are associated with mood disorders, but not more casual use.

Aside from marijuana use, we also identified housing instability and stigmatization as strong predictors of mood disorders among young BMSM. Worry about housing, history of homelessness, high experience of discrimination, and unfair treatment by police all had stronger associations with mood disorders than marijuana use. Overall these findings highlight the low socioeconomic status and high levels of adversity faced by young BMSM in Atlanta. This is important for setting the stage for interpreting the PrEP findings of this work; it is understandable that attending PrEP appointments and taking a pill every day with good adherence might be of lower priority than worrying about the basic securities of life: having a place to stay and having access to food.

PrEP uptake and discontinuation among young black men who have sex with men in EleMENt

At interim analysis 42% of the cohort had initiated PrEP through the study. This is a small underestimate of PrEP prevalence, because there were some participants who initiated PrEP during the study, but not through the study. There is not much context with which to compare this number. Most studies of PrEP have either been PrEP clinical trials/demo projects or observational population-level evaluations. PrEP trials cannot be

used to estimate uptake, because only those willing and interested are enrolled. Studies evaluating the uptake of PrEP in specific health systems or clinics cannot be used to determine a denominator of PrEP-eligible patients. In a survey of mostly white MSM in Washington, between 20% and 37% of people with PrEP indications reported current usage (66). In the EleMENt cohort, the inclusion criteria ensured that 100% of enrolled participants were PrEP-eligible based on CDC guidelines (54). Similarly, based on inclusion criteria—sexually active young BMSM in the south—we know that the cohort was at especially elevated risk for HIV compared to the general population of American MSM (1, 67). At baseline study visit, only 6% (19/298) of EleMENt participants reported being on PrEP. Thus, enrollment in the study, including PrEP education and access, moved PrEP use from 6% to 42%. This highlights the formidable structural barriers to PrEP use faced by young BMSM in Atlanta (15). We know that >42% PrEP coverage in high incidence populations will be needed to make a significant impact on overall HIV incidence in addition to improved virologic control in those with HIV ("Treatment as Prevention") (13, 14). From a public health standpoint, a goal of 100% PrEP uptake among this cohort would be appropriate, however respect and space for individuals' values and preferences is needed as well.

Of the 125 participants who started PrEP, more than half (63%) had at least 2 weeks lapse in usage. Thirty one percent had a final discontinuation. Based on the method of data collection, these two numbers are underestimates of the amount of discontinuation in the cohort. There is no consensus at this time as to the best way to measure PrEP persistence. Estimates of PrEP persistence in the literature have a huge range, at least partially due to the different definitions of persistence/discontinuation. **Table 8** shows a review of the literature of data on PrEP persistence with information on the different measures used (22, 68-76). In a cohort of young MSM in Chicago, 33% who had been on PrEP in the preceding 6 months had discontinued, by self-report (68).

Alternatively, when prescription refill records were used, adherence looked better, with between 74% and 92% coverage (22, 74). Similar to our findings of intermittent use, Doblecki-Lewis and colleagues identified different patterns of PrEP use: early discontinuation, intermittent use, and full use (76). Many of these studies showed that youth, black race, and MSM had some of the highest rates of discontinuation.

The effect of substance use on PrEP use

Across the PrEP continuum from uptake to first discontinuation to final discontinuation, marijuana use was consistently and independently associated with lower levels of PrEP use. Marijuana use was associated with 50% less uptake and almost twice as much discontinuation. Given the high prevalence of marijuana use and the high incidence of HIV in this demographic, this finding is important both from a public health standpoint and for clinicians managing PrEP for individuals who use marijuana. No prior research has evaluated the effect of marijuana use on PrEP uptake or persistence to date. While most research on the use or drugs to facilitate sex ("Chemsex") has focused on stimulants, GHB, and alcohol and their effect on risk behaviors and HIV/STI incidence (35-37, 77), less is known on how marijuana impacts these outcomes. Cohorts of MSM in Chicago, Rhode Island, Miami Beach, New Zealand, and Argentina have inconsistently associated marijuana use with HIV/STI risk behaviors and none have evaluated the effect on HIV/STI incidence (78-83). This is one of the primary outcomes of the overall EleMENt study; the impaired PrEP use identified in this study might lie in the causal pathway from marijuana use to HIV incidence.

The association found between marijuana use and lower PrEP use could be directly causal. Marijuana is known to be negatively associated with different aspects of the HIV care continuum among those with HIV infection (84). Although studies are small and occasionally inconsistent, the general trend shows that marijuana is associated

with less engagement in HIV care and more medication non-adherence. Marijuana can lead to apathy, demotivation, forgetfulness, and impaired decision making (85). All of these effects could explain difficulty in successful navigation of PrEP use in EleMENt, which required making an appointment, attending the appointment, providing documentation for patient assistance program forms, filling the prescription, adhering to a daily medication, and following up for repeat labs every 3 months. As noted above, with the high prevalence of marijuana use, there is likely a significant subset of the cohort with cannabis use disorder, which would further support causality between marijuana use and lower PrEP use. Part of the DSV-5 diagnostic criteria for cannabis use disorder includes failure to meet social and health obligations due to drug use. Further analyses of this data will include determining risks for uptake and discontinuation comparing different levels of marijuana use. At the very least, these data indicate that screening for marijuana use is important in PrEP programs with young BMSM as a way to risk stratify people at risk of low initiation and high risk of discontinuation. Further, it is biologically plausible that interventions aimed at reducing marijuana use and treating cannabis use disorder, including emerging pharmacotherapies (86), could improve PrEP use in this population.

The alternative interpretation is that marijuana use is a surrogate for a cluster of lived experiences, norms, and social circumstances that contribute to low PrEP use, rather than being directly causal. We controlled for important socioeconomic variables including age, education, insurance, housing stability, and problem-solving self-efficacy, but residual confounding remains a possibility. It is possible that marijuana use represents a lower level of self-care or health-mindedness among a subset of study participants. If this were the case, tobacco use should have a similar association with poorer PrEP outcomes, but in sensitivity analyses for both uptake and discontinuation,

the addition of 'tobacco use' to the models did not diminish the association of marijuana with the outcomes (**Supplementary Tables 3** and **4**).

The other substances evaluated, cocaine and alcohol, showed no effect on either PrEP uptake or discontinuation. The prevalence of cocaine use was relatively low at 14% and so there was not enough statistical power to detect anything besides a very large effect size. These data cannot rule out an effect of cocaine and other drugs on PrEP use. To date there are two studies evaluating the effect of substance use on PrEP outcomes among MSM in the United States and they show conflicting results (49, 87). For alcohol use, although the prevalence of risky use was higher (30%), there was only power of 0.54 (data not shown) to detect a 33% or greater change in the hazard for PrEP uptake. There was even less power to detect a change in PrEP discontinuation. One study evaluating PrEP adherence and binge alcohol use similarly found no effect, but was equally constrained by low power (49). The confidence intervals for both alcohol and cocaine use contain potentially large effect sizes in both directions. For now, substance use should certainly not be a barrier or restriction to PrEP use, but more data is needed to determine if people with heavy substance use require more attention and assistance to facilitate PrEP.

<u>The effect of mood disorders on PrEP use</u>

We identified no statistically significant effect of mood disorders on the use of PrEP between uptake and discontinuation. For both uptake and discontinuation models, the confidence intervals contain the possibility of large effect sizes both in the positive and negative directions. Although not conclusive, these results at least highlight the fact that untreated mood disorders are not a clear contraindication to offering PrEP to an eligible person. In order to increase power and to make results more generalizable, we combined anxiety and depression into one variable. Although there was considerable

overlap in these symptoms in the cohort (see **Supplementary Table 2**), if each disorder had differential effects on PrEP use, their combination would bias the HR toward the null. In sensitivity analyses (**Supplementary Tables 3** and **4**), evaluating anxiety and depression separately did show a notable trend toward different effects on PrEP use: anxiety was more strongly associated with *increased* PrEP uptake and depression with PrEP discontinuation. Based on these findings, future studies should evaluate the impact of anxiety and depression separately.

There was no evidence of interaction between substance use and mood disorders in either uptake or discontinuation models. Again, it is possible that the combination of anxiety and depression negated a true association with one or the other mood disorder; however, in sensitivity analyses (**Supplementary Tables 3** and **4**), there was still no statistical interaction when each mood disorder was evaluated with substance use separately. All three substance use×mood disorder cross-products were evaluated at the same time with a chunk test, which may have covered up interaction with only one of the substances. Based on the results found in these analyses, there is no evidence that the effect of marijuana (or cocaine or alcohol) on PrEP use is dependent on mental health status.

Sociodemographic predictors of PrEP use

The strongest predictor of PrEP uptake was self-efficacy for problem solving. Self-efficacy is one's belief in their ability to overcome challenges and succeed in completing a particular task. Bandura describes four factors that contribute to self-efficacy: 1) experience, [has someone been successful or failed in the past?]; 2) modeling [have they seen others like them succeed or fail?]; 3) social persuasion [are others encouraging and cheering them on or rooting against them?]; and 4) physiological factors [are they discouraged by feelings of anxiety, fear, trembling?] (88). One's self-

efficacy is innately tied to their environment and upbringing. The stigma and discrimination reported by many of the study participants—young gay black men of low socioeconomic status in the conservative south—is a strong contributor to low self-efficacy. Golub and colleagues similarly showed that high self-efficacy for PrEP adherence was associated with PrEP uptake in a cohort of MSM with access to PrEP (89). Although many of the contributors to low self-efficacy in this population are structural/societal and not easily remedied, self-efficacy can be improved with interventions designed to increase PrEP use among young MSM (90).

Higher educational attainment was also associated with increased PrEP uptake. In a similar way to self-efficacy, the mechanism is likely through improved skills navigating problems as well as better health literacy and health behaviors. Notably, both self-efficacy and education were independent predictors when controlling for one another, so each appears to contribute uniquely to increased PrEP uptake. We used an educational video and counseling to introduce PrEP to participants, but both may not have been appropriate for participants with less than a high school education. PrEP educational materials need to be targeted to the appropriate level of health literacy of the audience.

After participants started PrEP, neither self-efficacy nor education were significantly associated with PrEP persistence/discontinuation. There is potential for selection bias in this result, however, because the denominator for the PrEP discontinuation is itself influenced by the education and self-efficacy of participants who initiated PrEP. But it remains telling that while self-efficacy seemed important in navigating the PrEP uptake process, it did not protect participants from falling out of PrEP care.

Sexual risk behaviors and PrEP use

In bivariable analyses for PrEP uptake (**Table 4**) all measures of sexual HIV risk behavior showed a trend toward more PrEP uptake, though with varying statistical significance. In this cohort with no injection drug users, sexual risk behavior is ultimately the most proximal and important step before potential HIV transmission. Thus, it is encouraging that participants at greatest risk for HIV were also more likely to initiate PrEP. This is especially true for STI diagnosis, which is the most direct surrogate for HIV risk and also itself increases the chances of HIV transmission (91, 92). These results support existing efforts to integrate PrEP services into municipal and community STI and sexual/reproductive health clinics (23).

Among those who initiated PrEP, there was divergence in which measures of sexual risk were associated with persistence. Having an STI was paradoxically associated with more PrEP discontinuation (although P=0.09) whereas having more sexual partners were associated with persistence (in other words: having fewer partners was associated with more discontinuation). The STI findings were not seen in the sensitivity analysis looking at predictors of final discontinuation; so those with STIs were more likely to have a "discontinuation event" but ultimately restarted PrEP and were not more likely to stop overall. The effect of STIs on discontinuation is concerning and deserves being a high priority for further study.

The finding that fewer sex partners was predictive of PrEP discontinuation could be seen as "appropriate discontinuation," in that fewer partners indicates lower HIV risk which implies less indication for PrEP. We have previously described how HIV risk prediction scores are insensitive and perform poorly when applied to black MSM in the South (93). One problem is that young BMSM may underreport sexual risk and substance use behaviors (5, 38). The other is that even with lower HIV risk behaviors, BMSM have higher HIV incidence than white MSM (1) due to the higher prevalence of HIV in BMSM sexual networks (94, 95). At completion of the EleMENt study, we will be

able to evaluate whether report of fewer partners is truly associated with lower HIV incidence in the cohort. Indications for PrEP should be interpreted in the context of local HIV transmission patterns and intensity. Rather than focus PrEP indications exclusively on individual report of risk behaviors, it is more appropriate and potentially less stigmatizing, to make recommendations based on general demographic categories such as “MSM in the south”.

PrEP as entry-point to the healthcare system

Young black MSM in the United States have low access to- and engagement with-healthcare. In EleMENt only 38% (114/298) of participants reported visiting a primary care doctor in the prior year. Young BMSM often feel stigmatized by the medical system and have resultant medical mistrust that keeps them from seeking care, both for PrEP and for other medical conditions (96, 97). Through our PrEP program, we encountered mental health symptoms, undiagnosed chronic conditions (hypertension), and other acute non-PrEP non-STI related complaints in addition to significant socioeconomic problems (financial, housing, and food insecurity). Engaging participants in PrEP care is certain to lead to confrontation and diagnosis with other medical and social problems. PrEP programs have great potential to be a link between young BMSM and the larger healthcare system. By encountering culturally competent non-judgmental PrEP providers, BMSM may become more comfortable engaging in medical care. At the same time, however, there is an ethical obligation to either directly provide or refer patients to comprehensive care for all of the other problems encountered when providing PrEP. While HIV prevention is certainly important, it can feel narrow-minded to focus so much on this while participants struggle with severe depression/anxiety, homelessness, and food insecurity.

Limitations

The conclusions of these analyses are limited by the method of variable and outcome assessment and by the timing of exposure collection relative to the outcomes. The exposure variables and covariates were primarily self-report responses. When possible, composite variables including objective or biomarker validation were used, such as in the case of STI and substance use. Reporting on scales of mood disorders, alcohol use, and discrimination may have been incomplete or inaccurate. Besides the question on annual income, missing data was minimal. Income was not included in any multivariable models due to its missingness. Outcome assessment was also primarily by self-report. For PrEP uptake, participants estimated the first day they took a dose of PrEP. Study staff made these inquiries in a non-judgmental and open-ended manner to maximize a participant's comfort in reporting non-adherence.

Similarly, PrEP discontinuation was primarily determined through self-report. We used validation methods including TFV-DP levels, pharmacy refill records, prescription dates, and patient assistance program expiration dates, but these data were not always available. We erred on the side of overestimating PrEP persistence, so the estimates in this study are a "best case scenario" for PrEP use. Furthermore, when self-report was validated against TFV-DP levels (**Supplementary Table 6**) there was a low positive predictive value of self-report for protective drug levels. There are other variables that determine TFV-DP levels including how long ago PrEP was initiated, so there is likely some misclassification in this table. We conceptualized PrEP persistence as "taking PrEP at least a little bit" which is somewhat independent of TFV-DP levels. When the study is complete we will be able to see if low adherence PrEP use still reduced the incidence of HIV.

Finally, exposures for these analyses were all taken from the baseline study visit. As is notable from **Figure 1** and **Figure 2**, there were long delays for some between

baseline study visit and PrEP initiation (over 500 days for some). Of those who initiated PrEP, discontinuation occurred at most 2 years later. In a similar cohort of young MSM in Chicago, patterns of substance use remained stable over multiple years of follow up, however, changes in mood disorder symptoms were not assessed (98). While some variables don't change as much over time—age, education, insurance status, self-efficacy—substance use and mood disorders were assessed at follow up visits. Performing similar analyses using time-varying covariates would strengthen an argument for causality in these results.

CONCLUSION

Through these analyses, we have shown that although there is appropriate focus on expanding access to PrEP for young BMSM in the south, uptake and persistence of this highly efficacious intervention is inadequate, despite education and provision of PrEP. We identified a high prevalence of substance use and mood disorders, though only marijuana use had an impact on the use of PrEP. Instead, other variables including age, education, STI, number of partners, and self-efficacy had larger effects on the uptake and discontinuation of PrEP. Most studies of PrEP to date have evaluated either uptake or persistence. By investigating both in the same population, we discovered that the barriers and facilitators for uptake were different from discontinuation. This level of nuance will facilitate improved PrEP implementation efforts in this key population.

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TABLES/FIGURES

Table 1: Baseline characteristics of a cohort of HIV-negative young black men who have sex with men (N=298)

Variable	N (%)	Missing
Age at enrollment (median [IQR])	24 (22-27)	0
High School or higher education	220 (74)	1
Income <$15,000 annually	87 (31)	19
Worry about housing	150 (51)	1
Homeless in the past 6 months	25 (9)	6
Uninsured	111 (37)	1
Arrested ever	99 (34)	5
Food insecurity[1]	103 (50)	93
Anxiety symptoms, moderate to severe[2]	66 (23)	8
Diagnosis of anxiety	39 (13)	0
Depression symptoms, moderate to severe[3]	57 (20)	7
Diagnosis of depression	45 (15)	0
Diagnosis of anxiety or depression	58 (19)	0
Anxiety or depression, moderate to severe	86 (30)	7
Receiving treatment for anxiety or depression	16 (5)	0
Went to a primary care doctor past 12 months	114 (38)	0
Went to emergency department past 12 months	73 (24)	0
Hypertension	31 (10)	0
Diabetes	5 (2)	0
High cholesterol	9 (3)	0
No chronic diseases	209 (70)	0
Marijuana use[4]	202 (68)	0
Cocaine use[4]	41 (14)	0
Amphetamine use[4]	9 (3)	0
Illicit opioid use[4]	25 (8)	0
MDMA/ecstasy use[4]	20 (7)	0
Risky alcohol use[5]	88 (30)	0
Tobacco use[6]	63 (21)	0
STI in the past 12 months[7]	126 (42)	0
Number of anal or oral sex partners past 6 months (median [IQR])	3 (2-6)	5
Condomless anal sex past 6 months	229 (77)	0
Heard of PrEP prior to this study	256 (87)	5

IQR, interquartile range; MDMA, 3,4-methylenedioxy-methamphetamine; STI, sexually transmitted infection; PrEP, HIV pre-exposure prophylaxis

1. Defined as low or very low food security based on the U.S. Household Food Security Survey Module: Six-Item Short Form. Performed at 3-month visit, only 211 completed visit at interim analysis
2. Patient health questionnaire-8 scale (PQH-8)
3. Generalized anxiety disorder-7 scale (GAD-7)
4. Composite: self-report of past 6 month use or positive urine drug screen at enrollment
5. Alcohol use disorders identification test (AUDIT)
6. “Have you smoked over 100 cigarettes in your lifetime”
7. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment

Table 2: Associations between substance use and mood disorder symptoms and diagnoses among young black men who have sex with men

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Mood disorder symptoms or diagnosis	PR (95% CI)	P
Marijuana composite[1]							
Yes	196	65 (33)	1.50 (0.98-2.30)	.05	83 (42)	1.30 (0.93-1.81)	.11
No	95	21 (22)			31 (32)		
Cocaine composite[1]							
Yes	38	15 (39)	1.41 (0.90-2.18)	.15	20 (51)	1.39 (0.98-1.97)	.09
No	253	71 (28)			94 (37)		
MDMA composite[1]							
Yes	19	10 (53)	1.88 (1.18-3.00)	.02	12 (60)	1.61 (1.09-2.38)	.04
No	272	76 (28)			102 (37)		
Amphetamine composite[1]							
Yes	13	4 (31)	1.04 (0.45-2.40)	1.00*	7 (50)	1.31 (0.76-2.26)	.38*
No	278	82 (30)			107 (38)		
Opioids composite[1]							
Yes	23	7 (30)	1.03 (0.54-1.97)	.92	11 (46)	1.20 (0.76-1.90)	.46
No	268	79 (29)			103 (38)		
Marijuana UDS							
Yes	88	32 (36)	1.37 (0.96-1.96)	.09	39 (44)	1.22 (0.91-1.64)	.20
No	203	54 (27)			75 (36)		
Cocaine UDS							
Yes	18	6 (33)	1.14 (0.58-2.24)	.72	8 (44)	1.16 (0.68-1.98)	.61
No	273	80 (29)			276 (38)		
MDMA UDS							
Yes	0	0	-	-	0	-	-
No	298	86	-		114	-	
Amphetamine UDS							
Yes	7	1 (14)	0.48 (0.08-2.96)	.68*	2 (29)	0.73 (0.22-2.38)	.71
No	284	85 (30)			112 (39)		
Opioids UDS							
Yes	2	0	-	-	1 (50)	1.29 (0.32-5.21)	1.00*
No	289	86	-	-	113 (39)		
Marijuana ≥1 per week							
Yes	79	33 (42)	1.67 (1.18-2.37)	.005	44 (55)	1.68 (1.28-2.22)	.0005
No	212	53 (25)			70 (33)		
Marijuana ≥1 daily							
Yes	45	21 (47)	1.77 (1.21-2.57)	.006	27 (59)	1.67 (1.24-2.25)	.003
No	246	65 (26)			87 (35)		
Cocaine ≥1 per week							
Yes	7	3 (43)	1.47 (0.61-	.43*	4 (50)	1.30 (0.64-2.64)	.72

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Mood disorder symptoms or diagnosis	PR (95% CI)	P
			3.52)				
No	284	83 (29)			110 (38)		
MDMA ≥1 per week							
Yes	1	0	-	-	1 (100)	-	-
No	294	86	-	-	113 (39)		
Amphetamine ≥1 per week							
Yes	1	1 (100)	-	-	2 (100)	-	-
No	290	85 (29)			112 (38)		
Opioids ≥1 per week							
Yes	2	0	-	-	2 (67)	1.73 (0.77-3.91)	.56
No	289	86 (30)			112 (38)		
Heroin ≥1 per week							
Yes	0	0	-	-	1 (100)	-	-
No	291	86 (30)			113 (39)		
Alcohol ≥1 per week							
Yes	140	40 (29)	0.94 (0.66-1.34)	.72	55 (39)	1.00 (0.75-1.22)	1.00
No	151	46 (30)			59 (39)		
Alcohol ≥1 daily							
Yes	16	5 (31)	1.06 (0.50-2.24)	.88	8 (47)	1.23 (0.73-2.08)	.47
No	275	81 (29)			106 (38)		
At risk for AUD[2]							
Yes	87	30 (34)	1.26 (0.87-1.81)	.23	42 (48)	1.37 (1.02-1.82)	.04
No	204	56 (27)			72 (35)		
AUDIT mod-high risk of AUD[3]							
Yes	14	2 (14)	0.47 (0.13-1.72)	.24*	4 (27)	0.68 (0.29-1.59)	.32
No	277	84 (30)			110 (39)		
CDT Elevated[4]							
Yes	14	3	0.74 (0.27-2.06)	.76*	5 (33)	0.90 (0.43-1.88)	.78
No	221	64			82 (37)		
Alcohol use to forget about your problems							
Half the time or more	51	27 (53)	2.11 (1.49-2.99)	.0001	31 (61)	1.74 (1.31-2.32)	.0007
Almost never or sometimes	209	52 (25)			73 (35)		
MJ use to forget about your problems							
Half the time or more	79	35 (44)	1.69 (1.13-2.53)	.001	42 (53)	1.58 (1.13-2.21)	.008
Almost never or sometimes	107	28 (26)			36 (34)		
Cocaine use to forget about your problems							
Half the time or more	12	7 (58)	1.83 (0.84-3.99)	.13	7 (58)	1.28 (0.66-2.49)	.47

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Mood disorder symptoms or diagnosis	PR (95% CI)	P
Almost never or sometimes	22	7 (32)			10 (45)		
Age							
≥22	230	62 (27)	0.69 (0.47-1.00)	.06	86 (37)	0.80 (0.58-1.11)	.20
<22	61	24 (39)			28 (46)		
Education							
High school or more	216	57 (26)	0.67 (0.47-0.97)	.04	78 (36)	0.75 (0.55-1.00)	.06
Less than high school	74	29 (39)			36 (48)		
Income, annual							
≥$15000	190	51 (27)	0.78 (0.53-1.13)	.20	70 (37)	0.85 (0.63-1.16)	.31
<$15000	84	29 (35)			37 (43)		
Health insurance							
Yes	183	52 (28)	0.90 (0.63-1.30)	.58	70 (38)	0.94 (0.70-1.26)	.67
No	108	34 (31)			44 (40)		
Unemployed							
Yes	24	11 (46)	1.63 (1.01-2.62)	.07	13 (52)	1.39 (0.92-2.08)	.16
No	267	75 (28)			101 (38)		
Worry about housing							
A little or a lot	145	59 (41)	2.20 (1.49-3.26)	<.0001	75 (51)	1.90 (1.39-2.59)	<.0001
Not at all	146	27 (18)			39 (27)		
Homeless past 6 months							
Yes	22	11 (50)	1.86 (1.17-2.95)	.02	16 (73)	2.07 (1.53-2.80)	.0005
No	264	71 (27)			94 (35)		
Arrested ever							
Yes	97	28 (29)	0.95 (0.65-1.39)	.79	38 (39)	1.00 (0.83-1.22)	.99
No	191	58 (30)			75 (39)		
How many family members have you told you're MSM?							
None	45	17 (38)	1.37 (0.90-2.11)	.16	18 (40)	1.05 (0.71-1.55)	.83
Any	240	66 (28)			93 (38)		
Everyday discrimination scale							
≥15 (mod to high)	117	49 (42)	2.06 (1.42-2.97)	<.0001	62 (52)	1.82 (1.36-2.45)	<.0001
<15	167	34 (20)			48 (29)		
Ever been unfairly treated or abused by police							
Yes	92	36 (39)	1.57 (1.11-	.01	47 (50)	1.50 (1.13-1.99)	.00

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Mood disorder symptoms or diagnosis	PR (95% CI)	P
			2.24)				6
No	197	49 (25)			66 (33)		
I feel comfortable as a homosexual man							
Agree	247	70 (28)	0.87 (0.53-1.45)	.61	91 (37)	0.80 (0.55-1.16)	.27
Not agree	37	12 (32)			18 (46)		
I can solve problems if I try hard enough							
Not exactly true	70	28 (40)	1.54 (1.07-2.21)	.03	32 (46)	1.28 (0.94-1.75)	.13
Exactly true	219	57 (26)			78 (36)		

PR, prevalence ratio; CI, confidence interval; UDS, urine drug screen; MDMA, 3,4-methylenedioxy-methamphetamine; AUD, alcohol use disorder; AUDIT, alcohol use disorders identification test; CDT, carbohydrate deficient transferrin saturation; MJ, marijuana; MSM, man who has sex with men; LGBT, lesbian gay bisexual transgender.

*Indicates Fischer exact test

1) Composite: self-report of past 12 month use or positive urine drug screen at enrollment
2) AUDIT score ≥8
3) AUDIT score ≥16
4) CDT percent saturation ≥2.6%

Table 3: Adjusted model for associations between substance use and mood disorder symptoms among young black men who have sex with men

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Adjusted PR (95% CI)	P
Marijuana composite[1]						
Yes	196	65 (33)	1.50 (0.98-2.30)	.05	1.55 (0.99-2.42)	.05
No	95	21 (22)				
Cocaine composite[1]						
Yes	38	15 (39)	1.41 (0.90-2.18)	.15	1.53 (0.97-2.43)	.07
No	253	71 (28)				
MDMA composite[1]						
Yes	19	10 (53)	1.88 (1.18-3.00)	.02	2.04 (1.31-3.17)	.0015
No	272	76 (28)				
Amphetamine composite[1]						
Yes	13	4 (31)	1.04 (0.45-2.40)	1.00*		
No	278	82 (30)				
Opioids composite[1]						
Yes	23	7 (30)	1.03 (0.54-1.97)	.92	1.12 (0.58-2.16)	0.74
No	268	79 (29)				
Marijuana UDS						
Yes	88	32 (36)	1.37 (0.96-1.96)	.09	1.38 (0.95-2.00)	.09
No	203	54 (27)				
Cocaine UDS						
Yes	18	6 (33)	1.14 (0.58-2.24)	.72	1.24 (0.63-2.46)	.54
No	273	80 (29)				
MDMA UDS						
Yes	0	0	-	-		
No	298	86	-			
Amphetamine UDS						
Yes	7	1 (14)	0.48 (0.08-2.96)	.68*		
No	284	85 (30)				
Opioids UDS						
Yes	2	0	-	-		
No	289	86	-	-		
Marijuana ≥1 per week						
Yes	79	33 (42)	1.67 (1.18-2.37)	.005	1.61 (1.12-2.31)	.01
No	212	53 (25)				
Marijuana ≥1 daily						
Yes	45	21 (47)	1.77 (1.21-2.57)	.006	1.78 (1.21-2.62)	.004
No	246	65 (26)				
Cocaine ≥1 per week						
Yes	7	3 (43)	1.47 (0.61-3.52)	.43*		
No	284	83 (29)				
MDMA ≥1 per week						
Yes	1	0	-	-		
No	294	86	-	-		
Amphetamine ≥1 per week						

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Adjusted PR (95% CI)	P
Yes	1	1 (100)	-	-		
No	290	85 (29)				
Opioids ≥1 per week						
Yes	2	0	-	-		
No	289	86 (30)				
Heroin ≥1 per week						
Yes	0	0	-	-		
No	291	86 (30)				
Alcohol ≥1 per week						
Yes	140	40 (29)	0.94 (0.66-1.34)	.72	1.04 (0.71-1.53)	.85
No	151	46 (30)				
Alcohol ≥1 daily						
Yes	16	5 (31)	1.06 (0.50-2.24)	.88	1.17 (0.57-2.41)	.67
No	275	81 (29)				
At risk for AUD[2]						
Yes	87	30 (34)	1.26 (0.87-1.81)	.23	1.47 (1.01-2.13)	.04
No	204	56 (27)				
AUDIT mod-high risk of AUD[3]						
Yes	14	2 (14)	0.47 (0.13-1.72)	.24*	0.55 (0.15-1.98)	.36
No	277	84 (30)				
CDT Elevated[4]						
Yes	14	3	0.74 (0.27-2.06)	.76*		
No	221	64				
Alcohol use to forget about your problems						
Half the time or more	51	27 (53)	2.11 (1.49-2.99)	.0001	2.01 (1.39-2.89)	.0002
Almost never or sometimes	209	52 (25)				
MJ use to forget about your problems						
Half the time or more	79	35 (44)	1.69 (1.13-2.53)	.001	1.62 (1.08-2.45)	.02
Almost never or sometimes	107	28 (26)				
Cocaine use to forget about your problems						
Half the time or more	12	7 (58)	1.83 (0.84-3.99)	.13	1.70 (0.75-3.83)	.20
Almost never or sometimes	22	7 (32)				
Age						
≥22	230	62 (27)	0.69 (0.47-1.00)	.06	0.83 (0.54-1.29)	.41
<22	61	24 (39)				
Education						
High school or more	216	57 (26)	0.67 (0.47-0.97)	.04	0.73 (0.47-1.14)	.17
Less than high school	74	29 (39)				
Income, annual						
≥$15000	190	51 (27)	0.78 (0.53-1.13)	.20	0.89 (0.59-1.33)	0.56

Variable	Total (%)	Mood disorder symptoms	PR (95% CI)	P	Adjusted PR (95% CI)	P
<$15000	84	29 (35)				
Health insurance						
Yes	183	52 (28)	0.90 (0.63-1.30)	.58	0.93 (0.64-1.38)	.75
No	108	34 (31)				
Unemployed						
Yes	24	11 (46)	1.63 (1.01-2.62)	.07	1.60 (0.94-2.73)	.08
No	267	75 (28)				
Worry about housing						
A little or a lot	145	59 (41)	2.20 (1.49-3.26)	<.0001	2.03 (1.34-3.06)	.0008
Not at all	146	27 (18)				
Homeless past 6 months						
Yes	22	11 (50)	1.86 (1.17-2.95)	.02	1.76 (1.03-3.01)	.04
No	264	71 (27)				
Arrested ever						
Yes	97	28 (29)	0.95 (0.65-1.39)	.79	1.08 (0.73-1.58)	.70
No	191	58 (30)				
How many family members have you told you're MSM?						
None	45	17 (38)	1.37 (0.90-2.11)	.16	1.17 (0.73-1.86)	.52
Any	240	66 (28)				
Everyday discrimination scale						
≥15 (mod to high)	117	49 (42)	2.06 (1.42-2.97)	<.0001	1.96 (1.33-2.87)	.0006
<15	167	34 (20)				
Ever been unfairly treated or abused by police						
Yes	92	36 (39)	1.57 (1.11-2.24)	.01	1.66 (1.16-2.38)	.006
No	197	49 (25)				
I feel comfortable as a homosexual man						
Agree	247	70 (28)	0.87 (0.53-1.45)	.61	0.95 (0.56-1.63)	.86
Not agree	37	12 (32)				
I can solve problems if I try hard enough						
Not exactly true	70	28 (40)	1.54 (1.07-2.21)	.03	1.37 (0.93-2.01)	.11
Exactly true	219	57 (26)				

PR, prevalence ratio; CI, confidence interval; UDS, urine drug screen; MDMA, 3,4-methylenedioxy-methamphetamine; AUD, alcohol use disorder; AUDIT, alcohol use disorders identification test; CDT, carbohydrate deficient transferrin saturation; MJ, marijuana; MSM, man who has sex with men; LGBT, lesbian gay bisexual transgender.

*Indicates Fischer exact test

1) Composite: self-report of past 12 month use or positive urine drug screen at enrollment
2) AUDIT score ≥8
3) AUDIT score ≥16

4) CDT percent saturation ≥2.6%

Table 4: The effect of substance use and mood disorder symptoms on PrEP uptake in a cohort of young black men who have sex with men: Bivariable Cox proportional hazards model (N=279)

Variable	HR (95% CI)	P-value
Age ≥22 years	1.75 (1.07-2.86)	.03
High School or higher education	1.57 (1.01-2.45)	.05
Income ≥$15,000 annually	1.24 (.82-1.87)	.29
Worry about housing	0.79 (.55-1.14)	.21
Homeless in the past 6 months	0.97 (.51-1.85)	.92
Insured	0.97 (.66-1.41)	.86
Unemployed	0.91 (.46-1.79)	.78
Arrested ever	1.01 (.69-1.48)	.95
Depression symptoms, moderated to severe[1]	0.74 (.46-1.20)	.23
Diagnosis of depression	0.79 (.46-1.36)	.40
Anxiety symptoms, moderate to severe[2]	1.00 (.65-1.53)	1.00
Diagnosis of anxiety	1.05 (.62-1.77)	.87
Receiving treatment for anxiety or depression	1.07 (.39-2.98)	.90
Anxiety or depression, moderate to severe symptoms[3]	0.83 (.55-1.25)	.38
Self-efficacy[4]	2.01 (1.22-3.32)	.007
Every day discrimination scale ≥15	0.89 (.61-1.30)	.54
Hypertension	1.03 (.55-1.92)	.92
Marijuana use[5]	0.69 (.48-1.00)	.05
Cocaine use[5]	1.13 (.68-1.89)	.64
Amphetamine use[5]	1.75 (.65-4.74)	.27
Illicit opioid use[5]	1.30 (.70-2.41)	.41
MDMA/ecstasy use[5]	0.90 (.42-1.92)	.78
Risky alcohol use[6]	1.00 (.67-1.49)	.99
Tobacco use[7]	0.57 (.35-.95)	.03
STI in the past 12 months[8]	1.77 (1.23-2.55)	.002
≥3 oral/anal sex partners past 6 months	1.28 (.88-1.88)	.20
Condomless anal sex past 6 months	1.61 (.99-2.60)	.05
Heard of PrEP prior to this study	1.75 (.94-3.26)	.08
Year of study enrollment		
2015	1	
2016	0.83 (.49-1.41)	.45
2017	0.67 (.37-1.20)	.18

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; MDMA, 3,4-methylenedioxy-methamphetamine; STI, sexually transmitted infection

1. Patient health questionnaire-8 scale (PHQ-8)
2. Generalized anxiety disorder-7 scale (GAD-7)
3. Moderate or severe score on PHQ-8 or GAD-7
4. I can solve problems if I try hard enough
5. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
6. Alcohol use disorders identification test (AUDIT)
7. “Have you smoked over 100 cigarettes in your lifetime”
8. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment

Table 5: The effect of substance use and mood disorder symptoms on PrEP uptake in a cohort of young black men who have sex with men: Multivariable Cox proportional hazards model (N=279)

Variable	Model 1 aHR (95% CI)	P-value	Model 2 aHR (95% CI)	P-value	Model 3 aHR (95% CI)	P-value	Model 4 aHR (95% CI)	P-value
Anxiety or depression, moderate to severe symptoms[1]	**1.06 (0.68-1.65)**	**.80**					**1.13 (0.72-1.77)**	**.60**
Marijuana use[2]			**0.64 (0.43-0.95)**	**.03**			**0.63 (0.42-0.94)**	**.03**
Cocaine use[2]			**1.26 (0.72-2.20)**	**.42**			**1.26 (0.70-2.25)**	**.44**
Risky alcohol use[3]					**0.94 (0.62-1.43)**	**.79**	**0.97 (0.62-1.49)**	**.87**
Age ≥22 years	1.41 (0.82-2.41)	.21	1.36 (0.79-2.34)	.27	1.41 (0.82-2.42)	.21	1.37 (0.79-2.37)	.26
High School or higher education	1.70 (1.03-2.81)	.04	1.74 (1.05-2.90)	.03	1.68 (1.02-2.77)	.04	1.77 (1.06-2.95)	.03
Worry about housing	0.81 (0.54-1.23)	.33	0.83 (0.56-1.24)	.37	0.83 (0.56-1.24)	.36	0.81 (0.53-1.23)	.32
Insured	0.92 (0.60-1.40)	.68	0.94 (0.62-1.43)	.77	0.92 (0.60-1.40)	.70	0.94 (0.62-1.43)	.76
Self-efficacy[4]	2.02 (1.19-3.41)	.009	2.03 (1.20-3.41)	.008	2.01 (1.19-3.39)	.009	2.06 (1.22-3.48)	.007
STI in the past 12 months[5]	1.87 (1.28-2.71)	.001	1.93 (1.32-2.83)	.0006	1.87 (1.28-2.72)	.001	1.94 (1.33-2.83)	.0006
≥3 sex partners past 6 months	1.36 (0.92-2.01)	.12	1.45 (0.97-2.15)	.07	1.35 (0.92-2.00)	.13	1.46 (0.98-2.17)	.06

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; MDMA, 3,4-methylenedioxy-methamphetamine; STI, sexually transmitted infection

1. Moderate or severe score on PHQ-8 or GAD-7
2. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
3. Alcohol use disorders identification test (AUDIT) ≥8
4. I can solve problems if I try hard enough
5. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment

Model 1: Anxiety or depression symptoms
Model 2: marijuana and cocaine
Model 3: alcohol
Model 4: all 4 exposures
Likelihood ratio test for chunk test for interaction terms 0.12

Table 6: The effect of substance use and mood disorder symptoms on first PrEP discontinuation in a cohort of young black men who have sex with men: Bivariable Cox proportional hazards model

Variable	HR (95% CI)	P-value
Age <22 years	3.55 (2.05-6.15)	.0001
High School or higher education	0.63 (0.38-1.05)	.07
Income ≥$15,000 annually	0.94 (0.58-1.55)	.82
Worry about housing	1.03 (0.66-1.60)	.91
Homeless in the past 6 months	1.38 (0.63-3.00)	.42
Insured	1.04 (0.66-1.64)	.85
Unemployed	1.07 (0.49-2.32)	.87
Arrested ever	1.06 (0.66-1.70)	.81
Depression symptoms, moderated to severe[1]	1.12 (0.62-2.03)	.72
Diagnosis of depression	0.52 (0.24-1.13)	.10
Anxiety symptoms, moderate to severe[2]	1.05 (0.62-1.79)	.85
Diagnosis of anxiety	0.78 (0.39-1.56)	.48
Receiving treatment for anxiety or depression	0.16 (0.02-1.24)	.08
Anxiety or depression, moderate to severe symptoms[3]	1.03 (0.63-1.71)	.90
Self-efficacy[4]	1.35 (0.69-2.62)	.38
Every day discrimination scale ≥15	1.12 (0.71-1.77)	.64
Hypertension	0.76 (0.33-1.75)	.52
Marijuana use[5]	1.54 (0.95-2.47)	.08
Cocaine use[5]	1.08 (0.57-2.04)	.82
Amphetamine use[5]	1.38 (0.43-4.38)	.29
Illicit opioid use[5]	1.47 (0.73-2.94)	.28
MDMA/ecstasy use[5]	1.08 (0.44-2.69)	.86
Risky alcohol use[6]	0.64 (0.38-1.06)	.08
Tobacco use[7]	1.03 (0.57-1.87)	.92
STI in the past 12 months[8]	1.23 (0.79-1.91)	.37
<3 oral/anal sex partners past 6 months	1.92 (1.21-3.03)	.005
Condomless anal sex past 6 months	0.63 (0.36-1.10)	.11
Heard of PrEP prior to this study	0.65 (0.30-1.43)	.28
Year of study enrollment		
2015	1	
2016	0.92 (0.51-1.84)	.92
2017	0.74 (0.36-1.51)	.74

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; MDMA, 3,4-methylenedioxy-methamphetamine; STI, sexually transmitted infection

1. Patient health questionnaire-8 scale (PHQ-8)
2. Generalized anxiety disorder-7 scale (GAD-7)
3. Moderate or severe score on PHQ-8 or GAD-7
4. “Moderately” or “exactly true” response to: “I can solve problems if I try hard enough”
5. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
6. Alcohol use disorders identification test (AUDIT)
7. “Have you smoked over 100 cigarettes in your lifetime”
8. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment

Table 7. The effect of substance use and mood disorder symptoms on first PrEP discontinuation in a cohort of young black men who have sex with men: Multivariable Cox proportional hazards model

Variable	Model 1 aHR (95% CI)	P-value	Model 2 aHR (95% CI)	P-value	Model 3 aHR (95% CI)	P-value	Model 4 aHR (95% CI)	P-value
Anxiety or depression, moderate to severe symptoms[1]	**1.05 (0.61-1.79)**	**.87**					**1.08 (0.62-1.86)**	**.79**
Marijuana use[2]			**1.84 (1.10-3.08)**	**.02**			**1.92 (1.13-3.25)**	**.01**
Cocaine use[2]			**1.26 (0.62-2.57)**	**.53**			**1.35 (0.64-2.86)**	**.43**
Risky alcohol use[3]					**0.96 (0.55-1.67)**	**.88**	**0.78 (0.43-1.38)**	**.38**
Age <22 years	4.79 (2.54-9.01)	.0001	5.26 (2.79-9.93)	.0001	4.71 (2.44-9.10)	.0001	4.87 (2.53-9.38)	<.0001
High School or higher education	0.72 (0.41-1.28)	.27	0.70 (0.40-1.23)	.20	0.73 (0.41-1.28)	.27	0.71 (0.40-1.26)	.24
Worry about housing	1.15 (0.69-1.93)	.59	1.05 (0.64-1.74)	.85	1.16 (0.71-1.92)	.56	1.01 (0.60-1.71)	.96
Insured	0.99 (0.61-1.61)	.96	1.10 (0.67-1.81)	.70	0.99 (0.61-1.61)	.97	1.09 (0.66-1.81)	.74
Self-efficacy[4]	1.07 (0.53-2.15)	.85	0.98 (0.48-2.00)	.95	1.06 (0.53-2.14)	.86	0.92 (0.44-1.91)	.82
STI in the past 12 months[5]	1.51 (0.94-2.43)	.09	1.59 (0.99-2.56)	.05	1.50 (0.93-2.44)	.10	1.52 (0.94-2.47)	.09
<3 oral/anal sex partners past 6 months	2.35 (1.43-3.85)	.0008	2.50 (1.51-4.14)	.0004	2.33 (1.41-3.85)	.001	2.44 (1.47-4.05)	.0005

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; MDMA, 3,4-methylenedioxy-methamphetamine; STI, sexually transmitted infection

1. Moderate or severe score on PHQ-8 or GAD-7
2. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
3. Alcohol use disorders identification test (AUDIT) ≥8
4. I can solve problems if I try hard enough
5. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment

Model 1: Anxiety or depression symptoms
Model 2: marijuana and cocaine
Model 3: alcohol
Model 4: all 4 exposures
Likelihood ratio test for chunk test for interaction terms 0.97

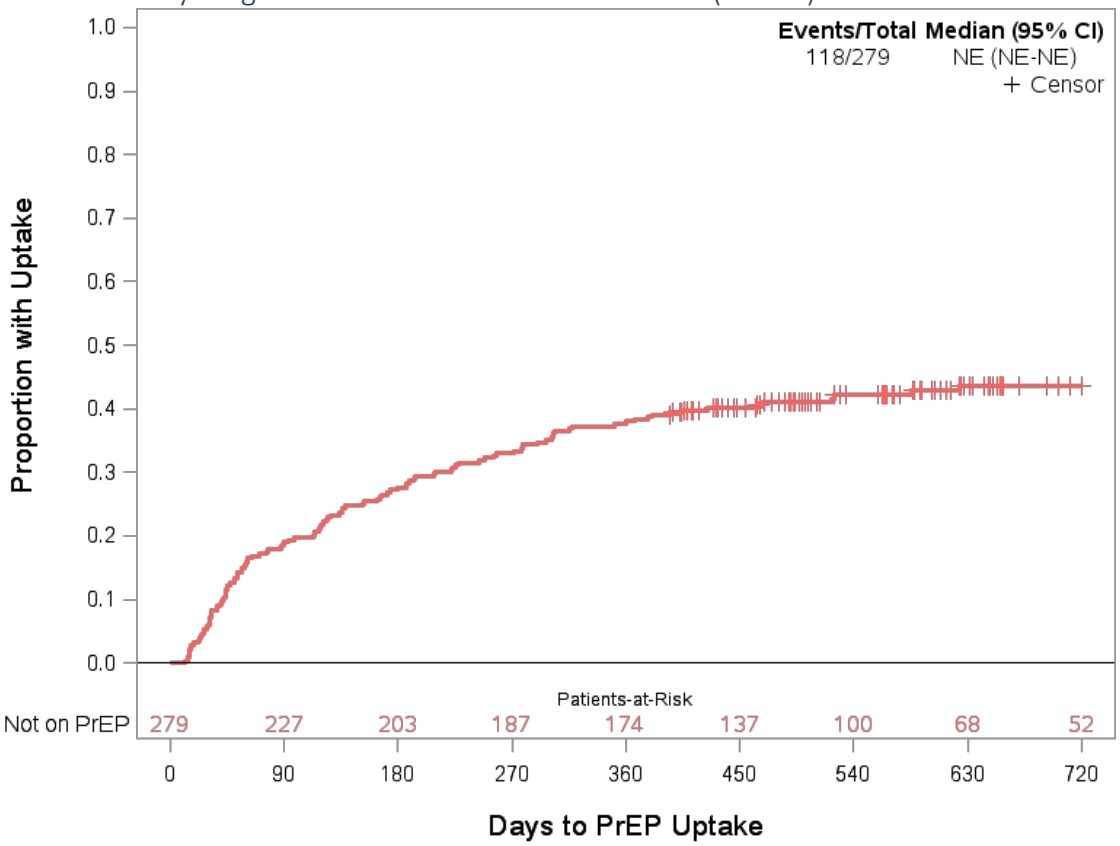
Table 8. Literature review of studies documenting PrEP persistence or discontinuation

Study	Period	Population	N	Study type	Persistence/DC measures	Associated variables	Reasons for DC
Morgan 2018	2015-2017	YMSM in Chicago	197	Prospective cohort questionnaire, PrEP not provided through study	65/197 (33%) who started PrEP in prior 6 months stopped use		Appts Insurance coverage Not at risk anymore
Chan 2016	2014-2015	MSM in Providence, St. Louis, Jackson, HIV/STI/LGBT clinics	267	Retrospective cohort of clinic records, clinic programs	73% retained 3 months, 60% retained 6 months	BMSM less retention at 3 months	
Hojilla 2018	2014-2015	Community sexual health clinic in San Francisco	268	Retrospective cohort chart review, clinic program	Discontinuation 4 m: 4% 7 m: 21% 13 m: 38%	STI → more discontinuation	
Gauthier 2019	2013-2018	Miami VA	79	Retrospective chart review, pharmacist lead PrEP program	43/79 (54%) on PrEP at end of study period		No longer at risk Lost to follow up
Rusie 2018	2012-2017	Chicago community health clinic	3451	Retrospective cohort chart review	43% retained for 12 or more months. 15% attended 4/4 annual visits	Uninsured status associated with fewer visits	
Dombrowski 2018	2014-2016	MSM in Seattle	307	Retrospective cohort chart review of county STI clinic	32% DC'd after starting		Monogamous Not at risk Lost to follow up
Van Epps 2018	2012-2016	VA nationwide	1086	Retrospective cohort	74% prescription coverage 44% DC'd in first year	Higher adherence: older, white, male	
Marcus 2016	2012-2015	MSM at Kaiser NorCal	972	Retrospective cohort	92% prescription coverage DC'd by 22%	Lower adherence: black race, higher copay, smoking More DC: female, drug/alcohol abuse	
Landovitz 2017	2014-2016	MSM in LA at LGBT based clinic	273	48-week clinical trial of TFV-level guided adherence support. PrEP provided	65% therapeutic at 48 weeks	Lower adherence: black race Higher adherence: older age group	
Dobleck-Lewis 2018		MSM in Miami, DC, San Francisco	554	PrEP demo project in STI clinics	66% full retention 23% intermittent retention 11% ELTF	Intermittent and ELTF: Miami, younger age, ELTF only: Black, sex work,	

unemployed

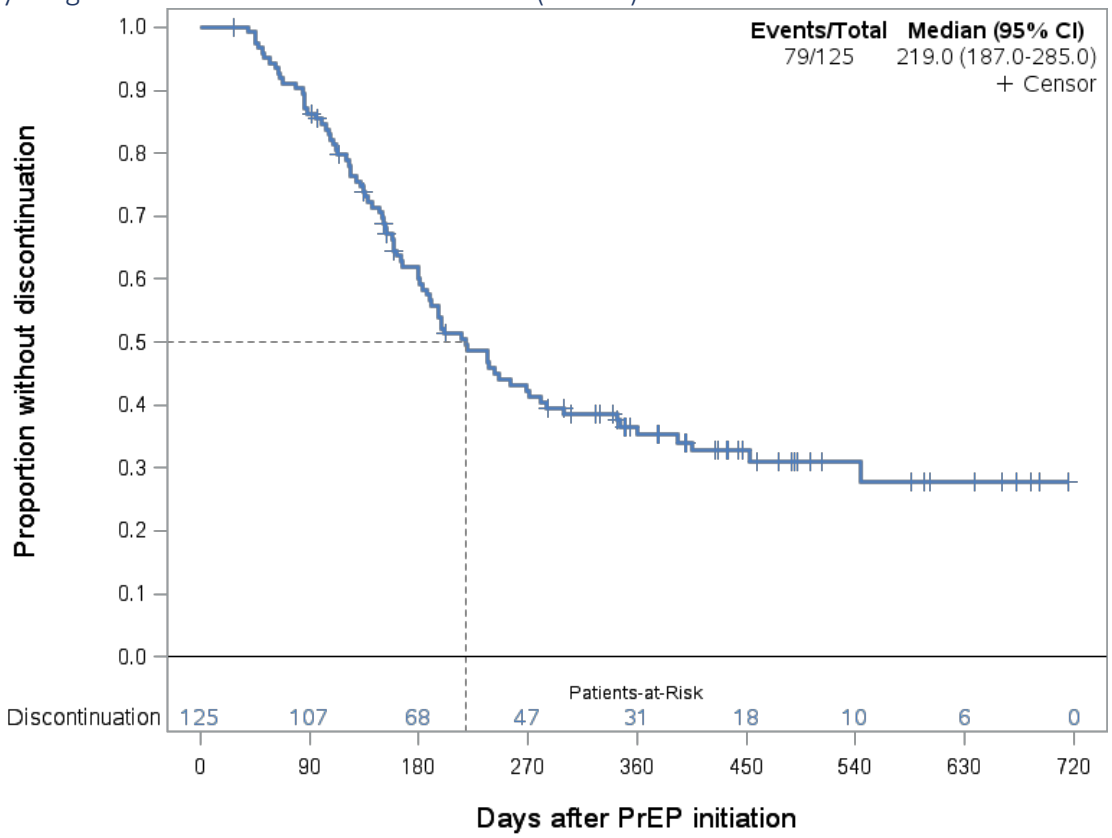
YMSM, young men who have sex with men; STI, sexually transmitted infection; LGBT, lesbian gay bisexual transgender; VA, Veterans Affairs Healthcare; ELTF, early loss to follow up; DC'd, discontinued

Figure 1: Cumulative incidence function of PrEP uptake as time from baseline study visit in a cohort of young black men who have sex with men (N=279)



Time to 25th percentile of uptake 152 (113-210) days

Figure 2: Kaplan-Meier survival curve of time to first PrEP discontinuation in a cohort of young black men who have sex with men (N=125)



Supplementary Table 1: Comparison of anxiety/depression diagnoses with moderate to severe symptoms of anxiety/depression among young black men who have sex with men

	Diagnosis of A/D	No diagnosis of A/D	Total
A/D[1]	30	56	86
No A/D[2]	25	180	205
Total	55	236	291 (7 missing)

A/D, anxiety or depression

1. Moderate to severe anxiety or depression on the GAD-7 or PHQ-8 scales, respectively
2. Absent or mild anxiety or depression on the GAD-7 or PHQ-8 scales, respectively

Supplementary Table 2: Overlap of moderate to severe anxiety and depression symptoms among young black men who have sex with men

	Depression + [1]	Depression - [2]	Total
Anxiety + [1]	37	29	66
Anxiety - [2]	19	205	224
Total	56	234	290

Missing data: 8 participants did not answer any questions from both scales

1. Moderate to severe anxiety or depression on the GAD-7 or PHQ-8 scales, respectively
2. Absent or mild anxiety or depression on the GAD-7 or PHQ-8 scales, respectively

Supplementary Table 3: Sensitivity analyses for the effect of substance use and mood disorder symptoms on PrEP uptake in a cohort of young black men who have sex with men: Multivariable Cox proportional hazards model

Variable	Model 1 aHR (95% CI)	P-value	Model 2 aHR (95% CI)	P-value	Model 3 aHR (95% CI)	P-value	Model 4 aHR (95% CI)	P-value
Anxiety or depression, moderate to severe symptoms[1]					**1.19 (0.75-1.87)**	**.46**		
Depression, moderate to severe[2]	**0.88 (0.52-1.48)**	**.62**						
Anxiety, moderate to severe[3]			**1.40 (0.88-2.24)**	**.16**			**1.51 (0.93-2.44)**	**.09**
Marijuana use[4]	**0.65 (0.43-0.97)**	**.03**	**0.61 (0.41-0.92)**	**.02**	**0.67 (0.44-1.01)**	**.05**	**0.65 (0.43-0.98)**	**.04**
Cocaine use[4]	**1.28 (0.72-2.29)**	**.40**	**1.22 (0.68-2.18)**	**.51**	**1.44 (0.79-2.62)**	**.24**	**1.42 (0.78-2.59)**	**.26**
Risky alcohol use[5]	**0.96 (0.62-1.49)**	**.87**	**0.96 (0.62-1.49)**	**.86**	**0.98 (0.63-1.51)**	**.93**	**0.98 (0.63-1.52)**	**.93**
Age ≥22 years	1.36 (0.78-2.34)	.28	1.36 (0.79-2.35)	.27	1.47 (0.84-2.55)	.18	1.46 (0.84-2.54)	.18
High School or higher education	1.73 (1.04-2.88)	.04	1.80 (1.08-3.00)	.02	1.68 (1.00-2.83)	.05	1.73 (1.03-2.90)	.04
Worry about housing	0.86 (0.57-1.31)	.48	0.81 (0.54-1.21)	.30	0.81 (0.53-1.23)	.32	0.81 (0.54-1.21)	.30
Insured	0.94 (0.62-1.43)	.77	0.94 (0.62-1.42)	.76	0.91 (0.59-1.38)	.65	0.91 (0.60-1.38)	.64
Self-efficacy[6]	2.02 (1.20-3.41)	.008	2.16 (1.27-3.66)	.004	1.99 (1.18-3.37)	.01	2.10 (1.24-3.58)	.006
STI in the past 12 months[7]	1.94 (1.33-2.84)	.0006	1.96 (1.34-2.87)	.0005	1.86 (1.27-2.72)	.001	1.89 (1.29-2.76)	.001
≥3 sex partners past 6 months	1.44 (0.97-2.15)	.07	1.45 (0.97-2.16)	.07	1.46 (0.98-2.18)	.06	1.89 (1.29-2.76)	.07
Tobacco use[8]					0.60 (0.34-1.04)	.07	0.57 (0.33-1.00)	.05

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; STI, sexually transmitted infection

1. Moderate or severe score on PHQ-8 or GAD-7
2. Patient health questionnaire-8 scale (PHQ-8)
3. Generalized anxiety disorder-7 scale (GAD-7)
4. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
5. Alcohol use disorders identification test (AUDIT) ≥8
6. I can solve problems if I try hard enough
7. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment
8. "Have you smoked over 100 cigarettes in your lifetime"

Model 1: depression symptoms
Model 2: anxiety symptoms
Model 3: tobacco use
Model 4: combined, using anxiety as mood disorder

Likelihood ratio test for chunk test for interaction between substance use and mood disorder terms
P=0.06

Supplementary Table 4. Sensitivity analyses for the effect of substance use and mood disorder symptoms on first PrEP discontinuation in a cohort of young black men who have sex with men: Multivariable Cox proportional hazards model

Variable	Model 1 aHR (95% CI)	P-value	Model 2 aHR (95% CI)	P-value	Model 3 aHR (95% CI)	P-value	Model 4 aHR (95% CI)	P-value
Anxiety or depression, moderate to severe symptoms[1]					**1.06 (0.61-1.83)**	**.84**		
Depression, moderate to severe[2]	**1.79 (0.88-3.65)**	**.11**					**1.80 (0.89-3.64)**	**.10**
Anxiety, moderate to severe[3]			**1.00 (0.55-1.79)**	**.99**				
Marijuana use[4]	**1.96 (1.16-3.32)**	**.01**	**1.91 (1.13-3.24)**	**.02**	**1.88 (1.11-3.20)**	**.02**	**1.92 (1.13-3.26)**	**.02**
Cocaine use[4]	**1.37 (0.66-2.87)**	**.40**	**1.37 (0.65-2.89)**	**.41**	**1.25 (0.56-2.78)**	**.58**	**1.26 (0.58-2.77)**	**.56**
Risky alcohol use[5]	**0.72 (0.40-1.30)**	**.27**	**0.77 (0.43-1.39)**	**.39**	**0.78 (0.43-1.41)**	**.41**	**0.73 (0.41-1.33)**	**.31**
Age <22 years	5.28 (2.73-10.21)	<.0001	4.91 (2.55-9.48)	<.0001	5.00 (2.58-9.68)	<.0001	5.42 (2.78-10.56)	<.0001
High School or higher education	0.75 (0.42-1.33)	.32	0.70 (0.39-1.25)	.23	0.71 (0.40-1.26)	.24	0.74 (0.42-1.32)	.32
Worry about housing	0.98 (0.58-1.64)	.93	1.03 (0.61-1.73)	.91	1.02 (0.61-1.71)	.95	0.98 (0.58-1.64)	.93
Insured	1.07 (0.65-1.76)	.78	1.11 (0.67-1.84)	.70	1.11 (0.67-1.85)	.69	1.09 (0.66-1.79)	.74
Self-efficacy[6]	1.05 (0.49-2.22)	.90	0.92 (0.44-1.90)	.82	0.94 (0.45-1.95)	.87	1.07 (0.50-2.27)	.86
STI in the past 12 months[7]	1.67 (1.01-2.75)	.04	1.53 (0.95-2.48)	.08	1.54 (0.95-2.49)	.08	1.69 (1.03-2.79)	.04
<3 oral/anal sex partners past 6 months	2.43 (1.47-4.04)	.0006	2.45 (1.48-4.07)	.0005	2.46 (1.48-4.08)	.0005	2.43 (1.47-4.05)	.0006
Tobacco use[8]					1.22 (0.61-2.42)	.58	1.24 (0.63-2.44)	.54

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; STI, sexually transmitted infection

1. Moderate or severe score on PHQ-8 or GAD-7
2. Patient health questionnaire-8 scale (PHQ-8)
3. Generalized anxiety disorder-7 scale (GAD-7)
4. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
5. Alcohol use disorders identification test (AUDIT) ≥8
6. I can solve problems if I try hard enough
7. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment
8. "Have you smoked over 100 cigarettes in your lifetime"

Model 1: depression symptoms

Model 2: anxiety symptoms
Model 3: tobacco use
Model 4: combined, using depression as the mood disorder
Likelihood ratio test for chunk test for interaction between substance use and mood disorder terms
P=0.77

Supplementary Table 5. The effect of substance use and mood disorder symptoms on final PrEP discontinuation in a cohort of young black men who have sex with men: Multivariable Cox proportional hazards model

Variable	Model 1 aHR	95% CI		P-value	Model 2 aHR	95% CI		P-value
Anxiety or depression, moderate to severe symptoms[1]	**2.08**	**0.92**	**4.72**	**.08**				
Depression, moderate to severe[2]					**1.96**	**0.67**	**5.73**	**.22**
Anxiety, moderate to severe[3]								
Marijuana use[4]	**2.94**	**1.31**	**6.59**	**.009**	**2.90**	**1.27**	**6.60**	**.01**
Cocaine use[4]	**2.03**	**0.82**	**5.02**	**.13**	**2.30**	**0.81**	**6.55**	**.12**
Risky alcohol use[5]	**0.42**	**0.17**	**1.05**	**.06**	**0.42**	**0.17**	**1.05**	**.06**
Age <22 years	3.41	1.51	7.69	.003	3.51	1.52	8.09	.003
High School or higher education	1.42	0.59	3.40	.44	1.32	0.54	3.22	.54
Worry about housing	1.21	0.54	2.71	.65	1.23	0.55	2.77	.61
Insured	1.16	0.52	2.58	.72	1.29	0.60	2.79	.52
Self-efficacy[6]	1.72	0.49	6.09	.40	1.78	0.47	6.72	.40
STI in the past 12 months[6]	0.89	0.43	1.85	.76	1.01	0.48	2.13	.97
<3 oral/anal sex partners past 6 months	1.92	0.95	3.91	.07	1.87	0.91	3.83	.09
Tobacco use[6]					0.74	0.26	2.16	.58

PrEP, HIV pre-exposure prophylaxis; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; STI, sexually transmitted infection

1. Moderate or severe score on PHQ-8 or GAD-7
2. Patient health questionnaire-8 scale (PHQ-8)
3. Generalized anxiety disorder-7 scale (GAD-7)
4. Composite: self-report of past 12 month use or positive urine drug screen at enrollment
5. Alcohol use disorders identification test (AUDIT) ≥8
6. I can solve problems if I try hard enough
7. Composite: self-report sexually transmitted infection (STI) past 12 months or positive STI test at enrollment
8. "Have you smoked over 100 cigarettes in your lifetime"

Supplementary Table 6: Comparison of self-reported PrEP adherence with tenofovir diphosphate dried blood spot levels in a subset of young black men who have sex with men taking PrEP

		TFV level >719 fmol/punch		
		Yes	No	Total
Reported taking ≥4 doses in last 7 days	Yes	27	23	50
	No	2	13	15
	Total	29	36	65

PrEP, HIV pre-exposure prophylaxis; TFV, tenofovir diphosphate level in dried blood spot
Positive predictive value: 27/50 (0.54), Negative predictive value: 13/15 (0.87), Sensitivity: 27/29 (0.93), Specificity: 13/36 (0.36)

Supplementary Figure 1: Kaplan-Meier survival curve of time to final PrEP discontinuation in a cohort of young black men who have sex with men