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How substance use, health insurance, and social determinants of health affect the HIV prevention continuum in Los Angeles, CA: Focus on Pre-Exposure Prophylaxis (PrEP) and Treatment as Prevention

Author

Shover, Chelsea Leigh

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How substance use, health insurance, and social determinants of health affect the HIV prevention continuum in Los Angeles, CA: Focus on Pre-Exposure Prophylaxis (PrEP) and Treatment as Prevention

A dissertation submitted in partial satisfaction of the

requirements for the degree of Doctor of Philosophy

in Epidemiology

by

Chelsea Leigh Shover

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ABSTRACT OF THE DISSERTATION

How substance use, sexual behavior, and social determinants of health affect the HIV prevention continuum in Los Angeles, CA: Focus on Pre-Exposure Prophylaxis (PrEP) and Treatment as Prevention

by

Chelsea Leigh Shover

Doctor of Philosophy in Epidemiology

University of California, Los Angeles 2018

Professor Pamina M. Gorbach, Chair

BACKGROUND: Recent advances in biomedical HIV prevention – including pre-exposure prophylaxis (PrEP) and treatment as prevention (TAsP) – are key to ending the HIV epidemic. The analysis examined how social factors that are strongly related to HIV incidence and treatment outcomes (e.g., substance use, access to healthcare, age, race/ethnicity, gender, and geographic location) may affect the HIV prevention continuum.

METHODS: Chapters 2 and 3 use data collected as part of clinical care at the Los Angeles LGBT Center. In Chapter 2, a cross-sectional study of HIV-negative men who have sex with

men (MSM) and transgender people who have sex with men (TGSM) who visited the Center between August 2015 and April 2017 examined how sexual history, substance use, and demographic factors were associated with initiating PrEP. In Chapter 3, records-based longitudinal study of patients prescribed PrEP at the Center evaluated discontinuation, HIV incidence, and loss to follow-up. Chapter 4 uses data from the mStudy to analyze the relationship between methamphetamine use (urine drug screen and self-reported frequency) patterns and viremia among HIV positive MSM of color.

RESULTS: Use of sex drugs, but not alcohol use, was associated with PrEP initiation among MSM and TGSM. Key demographic risks were associated with lower odds of PrEP initiation (Black or Latino race/ethnicity, younger age). About half of patients who started PrEP at the Center discontinued or were lost to follow-up. HIV incidence among those who discontinued was 1.4%, compared to 0.3% among those who were actively attending follow-up appointments. Persistence was highest for those receiving PrEP through a low-cost program, and lowest for younger people. Longitudinal patterns of frequent and/or recent methamphetamine use were associated with a detectable pattern of viremia.

CONCLUSION: Because younger people had lower PrEP initiation and more discontinuation compared to older people, strategies to support youth are key to PrEP's success for HIV prevention. The findings that methamphetamine was an obstacle to secondary HIV prevention but not necessarily to PrEP use highlight how facilitating PrEP use among people who use methamphetamine and other substances may be key to HIV prevention.

The dissertation of Chelsea Leigh Shover is approved.

Marjan Javanbakht

Sung-Jae Lee

Steven Shoptaw

Pamina M. Gorbach, Committee Chair

University of California, Los Angeles

2018

To my friends, my family, and my muses. Your love and support mean everything.

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"HIV pre-exposure prophylaxis initiation at a large community clinic: Differences between eligibility, awareness, and uptake" (Chapter 2) was submitted to the *American Journal of Public He*alth. Co-authors on this manuscript include: Marjan Javanbahkt, Steve Shoptaw, Sung-Jae Lee, Robert K. Bolan, Jeffrey Parsons, Jonathon Rendina, and Pamina M. Gorbach. CS, PG, MJ, SS, S-JL conceptualized the study, designed the study and analysis plan, and contributed to writing. CS conducted the analyses and wrote the manuscript. All co-authors interpreted results and critically revised the manuscript. The manuscript was undergoing peer review at the time of this dissertation filing.

"HIV Incidence and Risk of Discontinuation Among Patients Prescribed HIV Pre-Exposure Prophylaxis at a Large Community Clinic in Los Angeles, California" (Chapter 3) was submitted to *JAIDS.* All authors contributed to conceptualizing the study, interpreting results, and critically revising the manuscript. The manuscript was undergoing review at the time of this dissertation filing.

Data used in Chapters 2 and 3 were collected as part of clinical care at the Los Angeles LGBT Center. The analysis presented in Chapter 4 used data from the mStudy (MSM and Substances Cohort at UCLA Linking Infections, Noting Effects). Dr. Gorbach and Dr. Shoptaw are co-principal investigators of mStudy, which is funded by the National Institute on Drug Abuse (U01DA036267-05). The mStudy website is http://themstudy.org/.

Vita

May 2011	AB, English Harvard College Cambridge, MA
Oct. 2014 – June 2015	Graduate Student Researcher Behavioral Epidemiology Research Group University of California, Los Angeles Los Angeles, CA
June 2015 – July 2015	Epidemiologist / Public Health Investigator Public Health Foundation Enterprises Santa Barbara, CA
Aug. 2015 – June 2018	Epidemiology Assistant Los Angeles LGBT Center Los Angeles, CA
Sept. 2016 – June 2018	Teaching Assistant/Associate Introduction to Epidemiology; Behavioral Epidemiology; Methods of Scientific Communication; Applied Sampling University of California, Los Angeles Los Angeles, CA
Oct. 2014 – June 2016	Future Public Health Leaders Fellowship Fielding School of Public Health University of California, Los Angeles Los Angeles, CA
Oct. 2014 – June 2016	Dean's Leadership Grant Fielding School of Public Health University of California, Los Angeles Los Angeles, CA
Oct. 2014 – June 2017	Epidemiology Department Fellowship University of California, Los Angeles Los Angeles, CA
Oct. 2017 – June 2018	Dissertation Year Fellowship UCLA Graduate Division University of California, Los Angeles Los Angeles, CA

PUBLICATIONS

Cunningham N, Beymer M, Javanbahkt, M, Shover C, Bolan R. Concordance between self-reported STI history and biomedical results among men who have sex with men in Los Angeles, California. *Sex Transm Infect* 2017;93:514-519.

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PRESENTATIONS

Shover C, Shoptaw S, Javanbakht M, Bolan R, Gorbach P. Engagement in the HIV Pre-exposure Prophylaxis Care Cascade for MSM with High-Risk Non-Injection Substance Use: Results from a Sexual Health Clinic in Los Angeles, California. P0ster presented at the Center for Advancing Longitudinal Drug Abuse Research Summer Institute & International Global Health Conference, August 16, 2017. *J Neuroimmune Pharmacol*.

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Shover C, Pines H, Shoptaw S, Javanbakht M, Bolan R, Gorbach P. Joint Trajectories of Methamphetamine Use and Viral Load. Poster presented at Conference on Retroviruses and Opportunistic Infections. March 7, 2018.

Chapter 1. Introduction

Epidemiology of HIV in the United States

Human immunodeficiency virus (HIV) is spread primarily through sexual contact, but risk is not distributed evenly through the United States population.[1] Social determinants of health – e.g., age, race/ethnicity, gender, socioeconomic status, sexual orientation, housing status, geographic location – are strongly linked to both incident HIV infection and HIV treatment outcomes among those who become positive.[1–8] In practice, this means that certain communities in the United States face disproportionate burden of HIV; namely, LGBTQ (lesbian, gay, bisexual, transgender, and questioning) communities and communities of color, particularly Black or African Americans and Hispanics or Latinos.[1]

In the United States, over two thirds of new HIV diagnoses are among gay, bisexual, and other men who have sex with men (MSM).[3] In 2016, 44% of the 39,782 new HIV diagnoses in the United States were diagnosed in Black or African Americans, who comprise 12% of the population.[1] A quarter of new HIV diagnoses in 2016 were among Hispanic or Latino people, who make up 18% of the population.[1] While HIV rates among youth aged 13-24 have declined 18% between 2008 to 2014, young people remain at disproportionate risk of both HIV infection and poorer HIV treatment outcomes including unsuppressed viral load.[5] Racial disparities in HIV are pronounced among youth, with 55% of infections among young people occurring among Blacks and 24% occurring among Hispanics and Latinos.[5] Black MSM aged 25-34 saw a 30% increase in HIV diagnoses between 2011-2015 despite an overall decline in new infections of 8% among Black MSM during this period, where rate among youth remained high but stable.[9] HIV diagnoses among Hispanic and Latino MSM increased 13% between 2010-2014, with the rate

among youth aged 13-24 increasing 16% during this period.[10] Transgender women – people whose gender identity is female and whose sex at assigned at birth was male – have a high burden of HIV, with prevalence estimates between around 20%.[4] Limited data on HIV incidence among transgender men – people whose gender identity is male and sex assigned at birth was female – indicates that while HIV prevalence among all transgender men is relatively low, trans MSM have similar HIV risk behaviors to cisgender (non-transgender) MSM.[11–13] Studies of HIV risk among gender non-binary people – those who have a gender identity other than male or female – are rare in the literature. As among MSM, rates of new HIV diagnoses are highest among transgender people of color.[14]

Biomedical HIV prevention

Recent advances in biomedical HIV prevention hold the potential to end the HIV epidemic through primary and secondary prevention.[15] Chief among these are pre-exposure prophylaxis (PrEP) for those who are HIV negative and treatment as prevention (TasP) for those who are positive.[16–18] In 2012 the Food and Drug Administration approved daily oral tenofovir emtricitabine (TDF/FTC) as pre-exposure prophylaxis (PrEP) to prevent HIV acquisition.[19] Clinical trials have shown daily PrEP to be over 90% efficacious when taken consistently.[16,20] In 2014 the Centers for Disease Control and Prevention (CDC) released recommendations for providing PrEP to MSM who had a sexually transmitted infection (STI) or condomless anal intercourse (CAI) in the past six months, transgender women with male sex partners, and others at elevated risk.[21,22] The CDC estimates that, nationwide, 25% of MSM may be good candidates for PrEP based on the CAI and STI criteria, but PrEP uptake remains low.[22] Chapter 2 investigates how demographic and behavioral factors associated with HIV risk relate to PrEP initiation among MSM and transgender people with cisgender male partners.

Understanding the drivers of the discrepancy between those who may benefit from PrEP and those who currently use PrEP is important to designing interventions that can improve PrEP delivery. In addition to increasing uptake, supporting persistence is crucial to PrEP's effectiveness. Persistence on PrEP involves taking the pill regularly and attending follow-up appointments every three months for HIV/STI testing, monitoring for adverse effects, and refilling the prescription. The factors that impact PrEP use and persistence in community settings are not yet well understood.[21] Chapter 3 provides evidence for PrEP's effectiveness in a community setting and describes barriers and facilitators of PrEP persistence.

TAsP consists of providing antiretroviral therapy (ART) to individuals who are HIV positive, regardless of CD4 count. Early treatment supports the immune system and prevents illness by reducing viral load. [18] Additionally, early treatment provides secondary HIV prevention by reducing transmission, since individuals with undetectable viral load cannot transmit HIV to sex partners.[17,23] For TAsP to be an effective prevention strategy, people on ART need to take their medications as prescribed and remain virally suppressed. Chapter 4 examines how patterns of methamphetamine use in a cohort of HIV-positive MSM may influence viremia over time.

Substance use and HIV

Compared to the general U.S. population, a greater proportion of MSM report methamphetamine use, nitrite use, heavy alcohol use and use of club drugs, all of which are associated with both increased risk of HIV acquisition and decreased adherence to HIV treatment regimens.[24–33] Substance use behaviors associated with HIV acquisition are also prevalent among transgender women.[34] Methamphetamine, nitrites, and club drugs – including GHB, and

ecstasy/MDMA – are especially important to consider with primary HIV prevention because of their relationship with HIV acquisition[24–31,33,35] Many studies of substance use categorize methamphetamine and nitrites in the same category as club drugs. While use of these substances may co-occur, they may have heterogeneous effects on both HIV risk and use of PrEP. Use of methamphetamine can enhance and prolong sexual encounters, which elevates risk of HIV acquisition if people have more sex partners or rougher sex, and addiction is a possibility.[26,27,36,37] Nitrites are primarily used in sexual encounters, and club drugs for recreational or sexual purposes; while there is ample evidence of adverse events resulting from their use, there is less evidence for addiction to such substances.[28,38–42] Therefore, methamphetamine's relationship with biomedical HIV prevention may differ from club drugs Furthermore, there is recent evidence that MSM increase sexual risk behavior after recent methamphetamine use, suggesting that methamphetamine use may be an appropriate indication to start PrEP.[43] Chapter 2 considers nine combinations of sex drugs to identify heterogenous relationships between stimulants, nitrites, club drugs, and combinations thereof and PrEP eligibility, self-identified PrEP candidacy, and PrEP initiation.

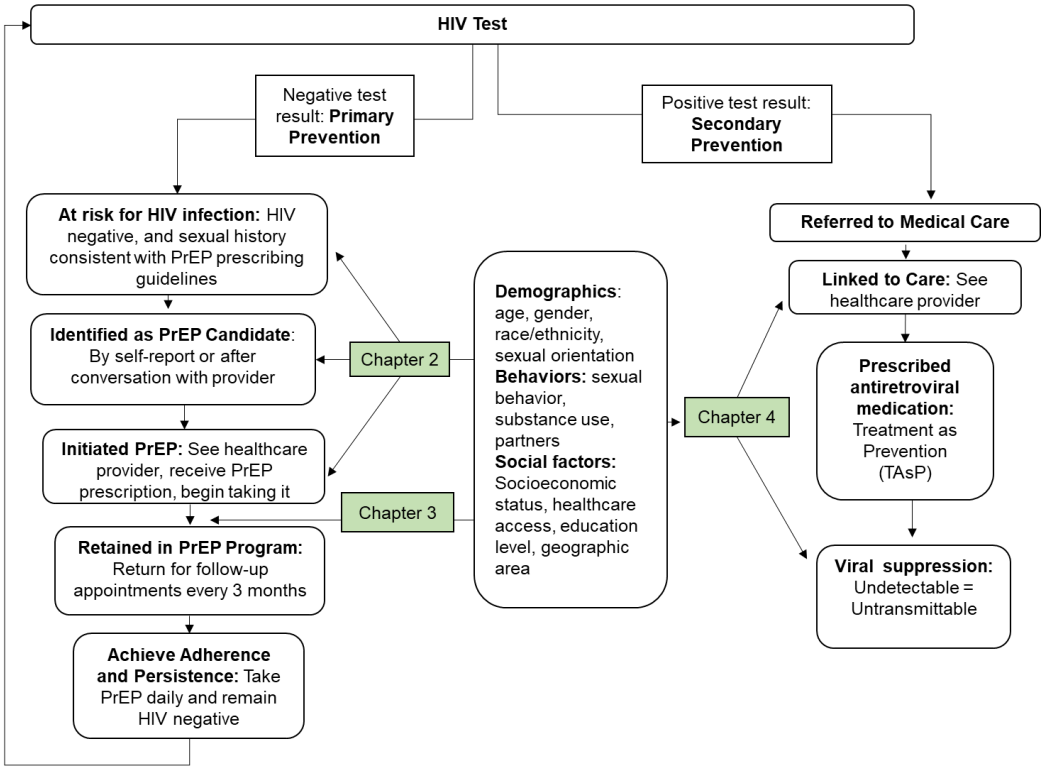
Methamphetamine use has important implications for secondary prevention as well, as it has been shown to be associated with decreased viral suppression among MSM on ART.[44] Chapter 4 investigates how different longitudinal patterns of methamphetamine use relate to HIV treatment outcomes, including patterns of viremia, and low CD4 count. By measuring both self-reported frequency in the past six months and urine drug screens (which detect use in the past three days), the analysis provides a comprehensive picture of trends in methamphetamine use over time. Chapter 4 uses group-based trajectory models (GBTMs) to identify underlying groups in frequency of methamphetamine use measured as a behavior and recent use as a biomarker. A

GBTM of HIV viral load identifies longitudinal patterns of viremia. Specifying a joint trajectory of methamphetamine toxicology and viremia identifies longitudinal relationships between pattern of methamphetamine use and viral load. Understanding these relationships can improve HIV management among MSM who use methamphetamine. In turn, this can ultimately improve the effectiveness of secondary HIV prevention.

Conceptual Model

The analysis is informed by a conceptual model based on PrEP continuums proposed by Liu et al and Kelley et al, and on the integrated HIV primary and secondary prevention continuum described by Horn et al. [15,45,46] **Figure 1.1** describes how biomedical HIV prevention may be influenced by demographic, behavioral, and social factors throughout steps in the prevention continuum.

Figure 1.1 Conceptual model of factors affecting primary and secondary biomedical HIV prevention



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Chapter 2. HIV Pre-Exposure Prophylaxis Initiation at a Large Community Clinic: Differences between Eligibility, Awareness, and Uptake

2.1 Abstract

Objectives: To characterize uptake of HIV pre-exposure prophylaxis (PrEP) in a community setting, and to identify disparities in PrEP use by demographic and behavioral factors associated with increased HIV risk.

Methods: A cross-sectional study of 16,105 men who have sex with men and transgender people visiting a large community clinic in Los Angeles between August 2015 and April 2017 was conducted using clinical care data.

Results: Two-thirds of patients met PrEP eligibility criteria, while 9% reported PrEP use. Using sex drugs, reporting both condomless anal intercourse and recent sexually transmitted infection, older age, and higher education level were associated with h igher odds of PrEP use given eligibility. Latino or Asian race/ethnicity and bisexual orientation were associated with lower odds of PrEP use given eligibility. Higher odds of perceived need were associated with demographic risk factors but PrEP use was not similarly elevated.

Conclusions: Discrepancies between PrEP eligibility, perceived need, and use reveal opportunities to improve PrEP delivery in community settings.

Policy implications: Efforts are needed to facilitate PrEP uptake in populations with highest HIV incidence.

2.2 Background

Taking HIV antiretroviral medication as pre-exposure prophylaxis (PrEP) is efficacious in preventing HIV infection.[1] Approved by the Food and Drug Administration (FDA) in 2012, oral daily tenofovir/emtricitibine (TDF/FTC) PrEP has been shown to reduce the risk of HIV acquisition by over

90% when taken at least four times per week.[2,3] The Centers for Disease Control and Prevention (CDC) recommend PrEP for individuals at elevated risk of HIV infection, and provides specific guidelines for PrEP use among men who have sex with men (MSM), and transgender people – that is, individuals whose gender identity differs from the sex they were assigned at birth.[3] In the United States, two-thirds of the approximately 40,000 new HIV infections annually occur among MSM, with highest incidence among young Black and Latino MSM. [4] HIV prevalence among transgender women (TW) is estimated to be 22%. [5] Limited data on transgender men who have sex with men (TMSM) suggests that while HIV prevalence is currently low compared to cisgender (non-transgender) MSM, TMSM engaging in HIV risk behaviors are an understudied but sizeable portion of transgender men. [6,7]

The CDC recommends PrEP for HIV negative MSM with a history of condom-less anal intercourse (CAI) or a sexually transmitted infection (STI) in the past six months, HIV negative TW who have cisgender male partners, and HIV negative individuals (all genders) with HIV positive partners.[3] Currently, the CDC does not provide targeted guidelines for transgender men, or for genderqueer people – individuals whose gender identity differs from assigned sex at birth but is not strictly male or female. Because transgender men and genderqueer people have typically been excluded from clinical research on PrEP, data from epidemiologic studies can provide evidence to develop PrEP recommendations for these populations.[5]

As PrEP becomes available outside of research settings, evaluation of its uptake and effectiveness in community settings is ongoing.[8-11] Despite PrEP's efficacy, population studies suggest PrEP use in community settings is low.[12-14] The CDC estimates that approximately 25% of MSM in the U.S. may be appropriate candidates for PrEP, but studies estimate real-world uptake to be under 5%.[12-14] Among TW, the gap between eligibility and uptake appears to be even larger.[5] This analysis aimed to characterize eligibility for PrEP, perceived need for PrEP, and PrEP initiation at a community clinic serving a large, diverse population of MSM and transgender people.

Lack of awareness, access barriers, stigma, cost, and concerns about side effects or drug interactions have been identified as barriers to PrEP initiation.[15,16] Among those who are aware of PrEP, a commonly cited barrier to initiation is self-perception as low risk for HIV infection despite having a history of STI or CAI with a partner of unknown HIV status.[15,17,18] A gap between hypothetical willingness and behavioral intention to use PrEP may also explain differences in need versus use.[19] Early studies of the PrEP continuum have documented differences in awareness of PrEP, eligibility for PrEP, willingness to use PrEP, and PrEP initiation related to social determinants of health, including age, race/ ethnicity, substance use.[12,20-24] These disparities are not yet well understood in community settings. Furthermore, increasing PrEP awareness, initiation, and supporting adherence for transgender people requires additional considerations.[5]

Non-injection substance use – including sex drugs (including stimulants, poppers, erectile dysfunction drugs (without prescription), and gamma-Hydroxybutyric acid), as well as heavy alcohol use – is associated with both increased risk of HIV acquisition and decreased adherence to HIV treatment regimens.[25-30] Use of sex drugs can impair decision-making and increase vulnerability to HIV infection by facilitating longer or more frequent sexual encounters. [26,28] Unlike condom use, effectively use of PrEP relies on planning but not necessarily in-the-moment actions, and may thus be a good option for individuals who use sex drugs. Evidence from some small studies suggest that stimulant use and alcohol use may affect PrEP initiation differently.[20,21]

Given the recent introduction of PrEP in the US, information about context of initiation and use are scanty. To contribute to the implementation science on PrEP, the objectives of this analysis were threefold: 1) identify correlates of reporting perceived need for PrEP among MSM and transgender people meeting the CDC's PrEP guidelines, 2) identify correlates of PrEP initiation among individuals who report perceived need for PrEP, and 3) determine relationship(s) between non-injection substance use and PrEP initiation. We hypothesized that significantly more individuals would be eligible than report perceived need, and significantly fewer individuals would initiate PrEP compared to those who report

perceived need. We further hypothesized that among those who are eligible for PrEP, demographic markers of increased HIV risk – younger age, Black or Latino race/ethnicity – would be associated with lower odds of PrEP initiation, while behavioral indicators of increased HIV risk – sex drug use, history of both CAI and STI – would be associated with greater odds of PrEP initiation.

2.3 Methods

The data for this study come from The Los Angeles LGBT Center, a federally qualified health center that provides free and low-cost HIV/STI testing through its Sexual Health Education Program (SHEP) at two clinics in West Hollywood and Los Angeles. When a patient undergoes HIV/STI testing, they first meet with a counselor who administers a 40-question risk assessment interview. PrEP-related questions were added to the risk assessment in August 2015. The analysis included the data collected in the medical record at the first visit of each unique client who visited SHEP between August 2015 and April 2017. A conceptual model based on HIV prevention continua informs this analysis (**Figure 1**).[22,31]

Records from patients who met the following criteria were included: 1) gender identity of cisgender man, transgender man, transgender woman, or genderqueer person; 2) gay or bisexual sexual orientation, or another sexual orientation and most recent partner was male; at least 18 years of age; 3) presumed HIV negative at baseline; 4) visited the Center during the study period. Individuals who tested HIV positive for the first time at their first visit during the study period were included because they answered PrEP questions prior to receiving HIV test results. Individuals who reported an established HIV infection, or a history of testing HIV positive, were excluded.

Age, birth sex, gender identity, sexual orientation, race/ethnicity (American Indian or Alaskan Native, Asian/Pacific Islander, Black, Latino/Hispanic, White, and other race including multiracial), and highest education level attained were reported by patients during the clinic's registration process. Other patient-level variables were collected via the counselor-administered risk assessment. Whether clients met the CDC's PrEP eligibility criteria was determined using questions about history of STI in the past year

and CAI in the past 90 days. Patients had a PrEP indication if they reported a history of sexually transmitted infection (gonorrhea, chlamydia, syphilis, HPV, Hepatitis B, or Hepatitis C) in the past year, or reported condomless anal intercourse (insertive or receptive) in the past 90 days. PrEP indication was coded as CAI only, STI only, or both CAI and STI. Substance use in the past 12 months was assessed by self-report in the risk assessment.

Perceived need for PrEP and PrEP use were measured with a scale used in prior research.[19] Likert scale responses to the question "Do you believe that you are currently an appropriate candidate for PrEP?" were collapsed to create binary perceived need categories of Yes and No/Unsure. To meResponses to the question "Have you ever taken PrEP?" were collapsed to create categories of Current Use and Former/Never Use.

Past year reports of sex drug use were categorized as follows: stimulants (including methamphetamine and MDMA/ecstasy), poppers, GHB, and erectile dysfunction drugs (without prescription), combinations of any two, and three or more. Heavy alcohol use was defined as five or more alcoholic beverages on at least five occasions in the past 30 days.

Statistical Methods

Chi-square tests were performed to assess independence of categorical variables. Bivariate logistic regression and multiple logistic regression models were created to assess relationships between independent variables and the three outcomes related to PrEP initiation.

Independent variables examined included: gender, sexual orientation, race/ethnicity, age group, education level, sex drug use, PrEP indication. Missing demographic variables were imputed from an individual's previous visit where available. Complete case analysis was used. Covariate-dependent missingness was investigated and significant predictors were included in the multivariable models. Year of visit was included in all models, and PrEP use was included in the perceived need model. All analyses were performed with SAS 9.4 (Cary, N.C.).

Ethics

The study received approval from the Institutional Review Board at the University of California, Los Angeles (IRB#17-000717).

2.4 Results

In total, 16,105 individuals met the inclusion criteria (**Table 1**). The majority (n = 15,678, 97%) were cisgender MSM, while 271 (1.7%) were TW, and less than 1% were TMSM or genderqueer people. More than half of the study population was over 30. The study population was ethnically diverse: 42% White, 33% Latino/Hispanic, 9% Asian/Pacific Islander, and 8% Black. Approximately half of participants had a college degree or higher. At first visit, 1,394 (9%) of individuals reported current PrEP use. Twenty-six percent of all participants (n=4,158) reported using any sex drug in the past year.

PrEP Eligibility

Sixty-seven percent (n=10,848) of all participants met at least one of the CDC criteria for PrEP eligibility, and 37% reported perceived need (**Table 1**). PrEP use was reported by 12% of individuals who met PrEP eligibility criteria, and 22% of those who reported perceived need. Of those who were eligible and reported perceived need (n=4,653), 25% reported current PrEP use.

In the bivariate and multivariable models, cisgender MSM had higher odds of PrEP eligibility than TMSM or genderqueer people, while the proportion of TW eligible for PrEP did not significantly differ from that of cisgender men. Individuals over 40 had lower odds of eligibility compared to those under 24. Asians had lower odds of PrEP eligibility compared to Whites, but eligibility did not otherwise differ significantly by race/ethnicity. Gay-identified individuals had highest odds of eligibility compared to bisexual-identified individuals or those with other sexual orientations. Controlling for demographic variables, heavy alcohol use and sex drug use were associated with significantly higher odds of eligibility for PrEP compared to those who reported non-heavy alcohol use, or no sex drug use, respectively.

Perceived Need

Among those who were eligible, perceived need for PrEP was associated with gender, age group, race/ethnicity, sexual orientation, indication, and sex drug use, but not education level or heavy alcohol use (**Table 2**). In the multivariable model, age group, sexual orientation, race/ethnicity, indication, education level, and sex drug use were significantly associated with perceived need for PrEP. Individuals 40 and older had lower odds of perceived need compared to younger individuals. Black (AOR = 1.3; 95%CI 1.1, 1.6) and Latino (AOR = 1.1; 95% CI 1.0, 1.3) individuals had significantly higher odds of perceived need than White individuals. Bisexual individuals and those with another sexual orientation had significantly lower odds of reporting perceived need compared to gay individuals. More individuals with a history of both STI and CAI reported perceived need for PrEP, compared to individuals who had STI only (AOR=0.6 95% CI 0.5, 0.7) or CAI only (AOR = 0.7; 95% CI 0.6, 0.8).

PrEP Use

Among those who were eligible, PrEP use was associated with gender, age group, race/ethnicity and sexual orientation, education level, indication, and sex drug use but not heavy alcohol use. In the multivariable model, PrEP use was associated with age group, race/ethnicity, sexual orientation, education level, indication, sex drug use, and heavy alcohol use (**Table 2**). Older individuals had higher odds of PrEP use compared to those under 24. Asian (AOR = 0.6; 95% CI 0.5, 0.8) or Latino (AOR = 0.5; 95% CI 0.4, 0.6) race/ethnicity was associated with lower odds of PrEP use compared to White ethnicity. Bisexual individuals and those with another sexual orientation had significantly lower odds of PrEP use compared to gay individuals. Individuals with a college degree or higher had 1.6 times the odds of PrEP use (95% CI 1.4, 1.8) compared to those with less than a college degree. Most patterns of sex drug use, except for stimulants only, were associated with higher odds of PrEP use in the adjusted model. Heavy alcohol use was associated with significantly lower odds of PrEP use (AOR = 0.7; 95% CI 0.6, 0.9).

Among those eligible but not using PrEP, race/ethnicity was a significant predictor of perceived need. Of the 9,208 individuals who met the criteria but were not currently taking PrEP, 41% reported perceived need. Both Black and Latino race/ethnicity were associated with higher odds of perceived need

in bivariate associations, compared to White race/ethnicity. In the multivariable model, Black individuals not on PrEP had significantly higher odds of reporting perceived need compared to White individuals not on PrEP (AOR 1.3; 95% CI 1.1, 1.6) (**Table 3**). Significantly lower odds of perceived need were associated with older age, bisexual or other sexual orientation, college degree or higher, and single PrEP indication.

2.5 Discussion

The study found PrEP use among individuals at elevated HIV risk was more common in this community based clinic population than previously reported in population-based surveys.[12,14] This may reflect the population that seek care and services at this Hollywood clinic – it is not a generalizable sample of MSM or TW but reflects those who choose to seek care in a gay identified setting that offers low cost and free care. Nevertheless, 9% is still low compared to the proportion who could benefit from PrEP (67% in this clinic). Though PrEP use was higher among those who met the CDC criteria and reported perceived need, there is an opportunity for improvement, as three quarters of this group were not using PrEP. In general, reporting more behavioral HIV risk factors was associated with greater perceived need for PrEP, and greater PrEP use. Those with a recent history of both CAI and STI were more likely to report perceived need and PrEP use, compared to those who reported only one indication. This is encouraging for maximizing HIV prevention resources allocated in Los Angeles County.

The relationship between PrEP initiation and substance use differed between sex drugs and heavy alcohol use. The finding that use of sex drugs was associated with higher odds of eligibility, perceived need, and PrEP use suggests that people who use sex drugs are aware of their increased HIV risk and willing to use PrEP. Still, the substantial gap between those who report perceived need and those who use PrEP may point to opportunities to increase PrEP services. Early longitudinal data suggests that stimulant users who do start PrEP may have equivalent adherence compared to non-users; thus, concerns about non-adherence should not discourage providing PrEP to individuals who use sex drugs.[32] Conversely, heavy

alcohol use was associated with lower odds of PrEP use, after controlling for demographics and sex drug use. These results may suggest a need for PrEP programs to adopt various strategies to engage people who use non-injection substances and recognize that alcohol is a substance associated with HIV risk.

Demographic correlates of perceived need versus PrEP use among eligible individuals highlighted disparities that could affect PrEP's effectiveness at a community-wide level. While Latino individuals had significantly higher odds of reporting perceived need compared to Whites, PrEP use was significantly lower. Blacks had significantly higher odds of reporting perceived need but similar odds of PrEP use compared to Whites. These are especially important finding because of the higher HIV incidence rates in Black and Latino communities.[33] Asians and Pacific Islanders had similar odds of perceived need compared to Whites but significantly lower odds of PrEP use. Though Asians account for a low percentage of HIV diagnoses in the United States, HIV incidence in Asians has been increasing.[33] Finally, Blacks and Latinos who met PrEP eligibility criteria but were not taking PrEP were more likely to report perceived need compared to Whites. The substantial gap between MSM and transgender people of color who view themselves as PrEP candidates and those who initiate PrEP suggests that PrEP is an acceptable intervention, but specific efforts to increase uptake of PrEP services are key to reducing HIV incidence. Younger age was associated with increased odds of perceived need and decreased odds of PrEP use. Like racial/ethnic disparities, this age disparity highlights an opportunity to improve access to PrEP for people who may, due to overlapping social determinants of health, face additional barriers to PrEP initiation, such as lack of insurance, or inconsistent access to a primary healthcare provider.

Compared to gay-identified individuals, PrEP-eligible bisexual individuals and those with another sexual orientation had lower odds of perceived need and PrEP use. Future studies evaluating PrEP initiation should collect more detailed information on how partnerships and exposures may differ by sexual orientation. Without this additional context, it is difficult to determine whether lower PrEP need and use among non-gay identified individuals represents a need for broader intervention.

Strengths

The study had several key strengths, including a large, ethnically diverse sample from a community clinic and does not represent a research study population that were incentivized to either adopt PrEP or participate in the study. To our knowledge, this is among the first PrEP analyses to include TMSM and genderqueer individuals. Though the analysis was underpowered to investigate demographic and behavioral correlates of PrEP initiation in transgender and genderqueer people, the differences in proportions of PrEP use in these groups compared to cisgender men point to the need for PrEP guidelines and programs for transgender and genderqueer people. Another strength was the ability to investigate substance use and PrEP initiation in a large sample and confirm findings from smaller studies that found associations between stimulant use and PrEP use.

Limitations

This analysis had several limitations. Since the sample was a convenience sample based on clinic attendance, findings may not be generalizable to individuals who do not access sexual healthcare or would not attend an LGBT-focused clinic. Differences in the time periods between the proxies and CDC criteria could have misclassified some individuals' PrEP eligibility. Additionally, answers to the CAI and STI questions may be subject to under-reporting. Finally, clinical nuance is lost in relying on the quantitative questions to assess PrEP eligibility. Based on these factors together, it is unclear whether the proxy would over-identify or under-identify individuals eligible for PrEP. PrEP use was assessed via self-report collected via a face to face interview, which may be subject to over-reporting due to social desirability bias. Some patients may have under-reported PrEP use due to stigma, but we expect this to be minimal in an LGBT-focused clinic that provides PrEP services. Some relevant substance use data were not available – including frequency of use, measures of dependence, and use of substances not included in the risk assessment (notably, cocaine). Furthermore, the 12-month timeframe for substance use report may misclassify those who used in the past year but not recently (e.g., 10 months ago versus past month). Ever use and recent use may inflence PrEP initiation differently in ways the design could not measure.

Finally, because the study was cross-sectional, temporality of substance use and PrEP use could not be established. By including only an individual's first visit, we could not distinguish between individuals who initiated PrEP by a later visit and those who never initiated PrEP during the study period.

Public Health Implications

By examining PrEP initiation in a community setting, this study identifies opportunities to improve PrEP delivery in non-research settings. Disparities in PrEP use among young MSM and transgender people of color suggest that while PrEP uptake is increasing generally, the same may not yet be true for populations with highest HIV incidence. Because PrEP is acceptable to those who use sex drugs, interventions providing PrEP services, including retention and adherence support, targeting these individuals have the potential to reduce HIV transmission.

Table 2.1 Baseline characteristics of study population, Aug 2015-April 2017, n=16,105.

	Eligible for PrEP		Currently taking PrEP		Total	
	n	%	n	%	n	%
Gender						
Cis men (who have sex with men)	10,603	98%	1,375	99%	15,678	97.3%
Trans women	172	2%	8	1%	271	1.7%
Trans men (who have sex with men)	12	0.1%	4	0.3%	50	0.3%
Genderqueer people	58	1%	7	1%	106	0.7%
Sexual Orientation						
Gay	8,997	83%	1,291	93%	12,929	80%
Bisexual	1,274	12%	79	6%	2,103	13%
Heterosexual	215	2%	5	0.4%	414	3%
Other	155	1%	8	1%	291	2%
Unknown	204	2%	11	1%	368	2%
Age group						
18-24	2,233	21%	129	9%	3,267	20%
25-29	3,095	29%	308	22%	4,405	27%
30-39	3,420	32%	559	40%	5,024	31%
40-49	1,319	12%	257	18%	2,050	13%
50+	781	7%	141	10%	1,359	8%
Race/Ethnicity						
American Indian or Alaska Native	35	0.3%	5	0.4%	50	0.3%
Asian/Pacific Islander	906	8%	91	7%	1,422	9%
Black or African American	773	7%	86	6%	1,246	8%
Hispanic/Latino	3,623	33%	284	20%	5,269	33%
Other	654	6%	82	6%	963	6%
White	4,601	42%	824	59%	6,844	42%
Unknown	253	2%	22	2%	411	3%
Education Level						
Less than college degree	4,191	39%	375	27%	6,022	37%
College degree and above	5,336	49%	899	64%	7,945	49%
Unknown	1,321	12%	120	9%	2,138	13%
Non-Injection Substance Use in the past 12 months						
Methamphetamine	648	6%	86	6%	779	5%
Nitrites	1,961	18%	374	27%	2,427	15%
GHB	522	5%	124	9%	595	4%
Ecstasy/MDMA	1,421	13%	245	18%	1,764	11%
Erectile dysfunction drugs without prescription	492	5%	138	10%	583	4%
Other prescription drug use without prescription	197	2%	24	2%	253	2%
Alcohol	8,091	75%	1,072	77%	11,733	73%
Heavy alcohol use (5 drinks or more, 5 times in the last	1,148	11%	133	10%	1,534	10%
Injection drug use ever	235	2%	24	2%	314	2%
Condomless anal intercourse, past 90 days	10,124	93%	1,208	87%	10,124	63%
STI, past year	2,651	24%	467	34%	2,651	16%
Reports Perceived Need for PrEP						
Yes	4,669	43%	1,270	91%	5,907	37%
Unsure	2,378	22%	26	2%	3,647	23%
No	2,660	25%	30	2%	4,813	30%
Unknown/Unreported	1,141	11%	68	5%	1,738	11%
PrEP Use						
Current	1,259	12%	1,394	100%	1,394	9%
Former	388	4%	--	--	496	3%
Never	8,820	81%	--	--	13,636	85%
Unknown/Unreported	381	4%	--	--	579	4%
Tested HIV positive at baseline visit	170	2%	1	0.1%	221	1%
Total	10,848	100%	1,394	100%%	16,105	100%

Table 2. Crude and adjusted odds ratios for correlates of reporting perceived need, and PrEP use among MSM and transgender people eligible for PrEP (n=10,848), Aug 2015-April 2017

	Perceived Need				PrEP Use			
	Crude OR	95% CI	Adjusted OR[a]	95% CI	Crude OR	95% CI	Adjusted OR[b]	95% CI
Gender	*p=0.03*		p=0.8		*p=0.01*		p=0.7	
Cis man (ref)	1.0	--	1.0	--	1.0	--	1.0	--
Transgender woman	0.7	(0.5, 1.0)	0.9	(0.6, 1.5)	0.3	(0.2, 0.7)	0.9	(0.3, 2.7)
Other gender	0.6	(0.4, 1.0)	0.8	(0.4, 1.5)	0.8	(0.4, 1.9)	1.5	(0.6, 3.9)
Age	*p=0.0005*		*p=0.009*		*p<0.0001*		*p<0.0001*	
18-24 (ref)	1.0	--	1.0	--	1.0	--	1.0	--
25-29	1.1	(1.0, 1.3)	1.0	(0.9, 1.2)	1.9	(1.6, 2.4)	1.6	(1.2, 2.0)
30-39	1.2	(1.1, 1.4)	1.0	(0.9, 1.1)	3.3	(2.7, 4.1)	2.8	(2.2, 3.5)
40-49	1.1	(1.0, 1.3)	0.8	(0.7, 1.0)	4.3	(3.4, 5.4)	3.3	(2.5, 4.3)
50+	0.9	(0.8, 1.1)	0.7	(0.6, 0.9)	3.5	(2.7, 4.6)	2.5	(1.9, 3.5)
Ethnicity	*p=0.033*		*p=0.01*		*p<0.0001*		*p<0.0001*	
White (ref)	1.0	--	1.0	--	1.0	--	1.0	--
Asian/PI	0.9	(0.8, 1.1)	1.1	(0.9, 1.3)	0.5	(0.4, 0.7)	0.6	(0.5, 0.8)
Black	1.1	(1.0, 1.4)	1.3	(1.1, 1.6)	0.6	(0.5, 0.8)	0.8	(0.6, 1.0)
Hispanic	0.9	(0.8, 1.0)	1.1	(1.0, 1.3)	0.4	(0.3, 0.4)	0.5	(0.4, 0.6)
Other	0.9	(0., 1.0)	0.9	(0.8, 1.1)	0.7	(0.5, 0.9)	0.8	(0.6, 1.1)
Sexual orientation	*p<0.0001*		*p=0.02*		*p<0.0001*		*p<0.0001*	
Gay (ref)	1.0	--	1.0	--	1.0	--	1.0	--
Bisexual	0.7	(0.6, 0.8)	0.9	(0.8, 1.0)	0.4	(0.3, 0.5)	0.4	(0.3, 0.6)
Other	0.6	(0.5, 0.7)	0.7	(0.5, 1.0)	0.2	(0.1, 0.4)	0.2	(0.1, 0.5)
Education Level	p=0.3		*p=0.02*		*p<0.0001*		*p<0.0001*	
Less than college degree ((	1.0	--	1.0	--	1.0	--	1.0	--
College degree or more	1.0	(1.0, 1.1)	0.9	(0.8, 1.0)	2.1	(1.8, 2.4)	1.6	(1.4, 1.8)
PrEP Indication	*p<0.0001*		*p<0.0001*		*p<0.0001*		*p<0.0001*	
STI and CAI (ref)	1.0	--	1.0	--	1.0	--	1.0	--
STI only	0.4	(0.3, 0.5)	0.6	(0.5, 0.7)	0.3	(0.3, 0.4)	0.3	(0.2, 0.4)
CAI only	0.5	(0.5, 0.6)	0.7	(0.6, 0.8)	0.4	(0.3, 0.4)	0.4	(0.3, 0.5)
Sex Drug Use	*p<0.0001*		*p<0.0001*		*p<0.0001*		*p<0.0001*	
None (ref)	1.0	--	1.0	--	1.0	--	1.0	--
Stimulants only	1.2	(1.0, 1.4)	1.2	(1.0, 1.5)	1.2	(0.9, 1.5)	1.1	(0.9, 1.4)
Nitrites only	1.5	(1.3, 1.8)	1.3	(1.1, 1.6)	1.9	(1.6, 2.3)	1.7	(1.4, 2.1)
ED Drugs only	1.5	(1.1, 2.1)	1.1	(0.7, 1.8)	3.7	(2.5, 5.4)	2.7	(1.8, 4.1)
GHB only	1.7	(0.9, 3.2)	1.5	(0.7, 3.2)	3.3	(1.7, 6.7)	2.9	(1.4, 6.1)
Stimulants and Nitrite	1.5	(1.3, 1.9)	1.5	(1.2, 1.9)	1.7	(1.3, 2.2)	1.6	(1.2, 2.2)
Stimulants and ED	2.0	(1.1, 3.7)	1.3	(0.6, 2.8)	4.1	(2.1, 7.8)	2.9	(1.4, 6.1)
Stimulants and GHB	1.1	(0.8, 1.7)	0.8	(0.5, 1.3)	2.3	(1.5, 3.7)	2.1	(1.2, 3.4)
2 drugs, Non stimulant	2.4	(1.6, 3.5)	1.7	(1.1, 2.9)	3.8	(2.5, 5.7)	2.8	(1.8, 4.3)
Poly (3 or more)	2.7	(2.1, 3.4)	2.0	(1.5, 2.6)	3.2	(2.5, 4.1)	2.7	(2.0, 3.5)
Heavy Alcohol Use	p=0.33		p=0.7		p=0.11		p=0.01	
5 drinks or more, 5 times in the last 30 days	1.1	(0.9, 1.2)	1.0	(0.8, 1.2)	0.9	(0.7, 1.0)	0.7	(0.6, 0.9)
Year of Visit	*p= 0.0009*		*p=0.007*		*p=0.004*		*p=0.003*	
2015	1.0	--	1.0	--	1.0	--	1.0	--
2016	0.9	(0.8, 0.9)	0.9	(0.8, 0.9)	1.0	(0.9, 1.1)	1.1	(0.9, 1.3)
2017	1.0	(0.8, 1.1)	0.8	(0.7, 1.0)	1.3	(1.1, 1.6)	1.4	(1.2, 1.8)
PrEP Use	*p<0.0001*		*p<0.0001*					
Current	46.0	(32.9, 64.2)	45.1	(31.7, 64.2)	--	--	--	--

[a] 2,538 observations were excluded due to missing values

[b] 1,867 observations were excluded due to missing values

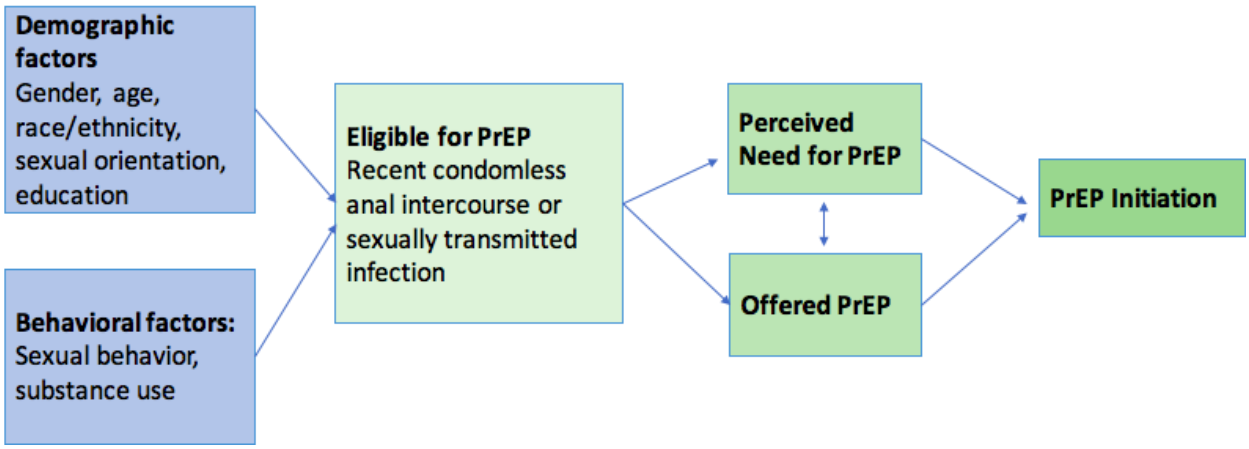
Table 3. Characteristics of MSM and TGSM attending the Los Angeles LGBT Center's Sexual Health Program who meet PrEP eligibility criteria and are not taking PrEP, (n=9,208) August 2015-April 2017

			Perceived Need			
					Adjusted	
	n	%[a]	Crude OR	95% CI	OR[b]	95% CI
Gender			p=0.1		p=0.8	
Cis man (ref)	8,989	85%	1.0	--	1.0	--
Transgender woman	159	92%	0.9	(0.6, 1.2)	0.90	(0.6, 1.5)
Other gender	60	86%	0.6	(0.3, 1.0)	0.80	(0.4, 1.5)
Age			*p<0.0001*		*p=0.002*	
18-24 (ref)	2,047	92%	1.0	--	1.0	--
25-29	2,701	87%	1.0	(0.9, 1.2)	1.0	(0.9, 1.1)
30-39	2,795	82%	0.9	(0.8, 1.1)	1.0	(0.9, 1.1)
40-49	1,026	78%	0.8	(0.7, 0.9)	0.8	(0.7, 0.9)
50+	639	82%	0.6	(0.5, 0.7)	0.7	(0.6, 0.9)
Ethnicity			*p=0.0002*		*p=0.007*	
White (ref)	3,719	81%	1.0	--	1.0	--
Asian/PI	784	87%	1.1	(0.9, 1.3)	1.1	(0.9, 1.3)
Black	660	85%	1.4	(1.2, 1.7)	1.4	(1.1, 1.7)
Hispanic	3,247	90%	1.2	(1.1, 1.3)	1.1	(1.0, 1.3)
Other	590	86%	1.0	(0.8, 1.2)	1.0	(0.8, 1.2)
Sexual orientation			*p=0.003*		*p=0.02*	
Gay (ref)	7,530	84%	1.0	--	1.0	--
Bisexual	1,158	91%	0.9	(0.8, 1.0)	0.9	(0.8, 1.0)
Other	346	94%	0.7	(0.6, 0.9)	0.7	(0.5, 1.0)
Education Level			*p=0.0008*		*p=0.02*	
Less than college degree (ref)	3,699	88%	1.0	--	1.0	--
College degree or more	4,331	81%	0.9	(0.8, 0.9)	0.9	(0.8, 1.0)
Sex Drug Use			*p<0.0001*		*p<0.0001*	
None (ref)	6,646	88%	1.0	--	1.0	--
Stimulants only	745	86%	1.2	(1.0. 1.4)	1.3	(1.0, 1.5)
Nitrites only	822	80%	1.4	(1.2, 1.6)	1.3	(1.1, 1.6)
ED Drugs only	99	69%	1	(0.6, 1.5)	1.2	(0.7, 1.9)
GHB only	31	66%	1.5	(0.7, 3.0)	1.7	(0.8, 3.6)
Stimulants and Nitrite	369	81%	1.5	(1.2, 1.8)	1.5	(1.2, 2.0)
Stimulants and ED	30	67%	1.4	(0.7, 2.8)	1.3	(0.6, 2.8)
Stimulants and GHB	33	28%	0.9	(0.5, 1.3)	0.8	(0.5, 1.3)
2 drugs, Non stimulant	84	68%	1.7	(1.1, 2.7)	1.8	(1.1, 3.0)
Poly (3 or more)	265	69%	2.2	(1.7, 2.9)	2.0	(1.5, 2.7)
Heavy Alcohol Use			p=0.09		p=0.9	
5 drinks or more, 5 times in the last 30 days	1,006	88%	1.1	(1.0, 1.3)	1.0	(0.9, 1.2)
PrEP Indication			*p<0.0001*		*p<0.0001*	
STI and CAI (ref)	1,437	75%	1.0	--	1.0	--
STI only	648	90%	0.5	(0.4, 0.6)	0.6	(0.5, 0.7)
CAI only	7,123	87%	0.7	(0.6, 0.8)	0.7	(0.7, 0.8)
Year			*p<0.0001*		*p=0.003*	
2015 (ref)	3,516	88%	1.0	--	1.0	--
2016	4,642	86%	0.8	(0.8, 0.9)	0.8	(0.8, 0.9)
2017	1,050	73%	0.8	(0.7, 1.0)	0.8	(0.7, 1.0)
Total	9,208	85%				

[a]Percent not currently taking PrEP, of total in each category who meet eligibility criteria (see Table 1 for row totals

[b] 1,987 observations were excluded due to missing values

Figure 2.1 Conceptual model of PrEP initiation in community settings



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Chapter 3. HIV Incidence and Risk of Discontinuation Among Patients Prescribed HIV Pre-Exposure Prophylaxis in a Community Clinic in Los Angeles, California

3.1 Abstract

Objectives: To assess effectiveness of pre-exposure prophylaxis (PrEP) in a large community clinic and identify correlates of PrEP discontinuation.

Setting: A longitudinal chart review of patients prescribed PrEP at the Los Angeles LGBT Center between March 2014 and February 2017.

Methods: Patients were followed for at least six months, and PrEP status (active, discontinued, or lost to follow-up) was assessed as of September 2017. We compared HIV incidence (as of March 2018) among active PrEP patients versus patients who discontinued PrEP (Fisher's exact test). Factors influencing PrEP discontinuation were assessed using multinomial logistic regression.

Results: Of 1,715 cisgender men and transgender women who initiated PrEP during the study period, 47% were active at the end of the analysis period, 37% had discontinued, and 16% were lost to follow-up. HIV incidence differed significantly between those had discontinued PrEP (1.4%, n=9) compared to 0.3% incidence (n=2) among active PrEP patients. Patients aged 18-24 had higher risk of discontinuation (Adjusted risk ratio = 1.41, 95% CI 1.21-1.57) compared to those aged 41-50. Compared to patients with Medicaid, risk of discontinuation was significantly higher among those with private insurance (ARR = 1.25, 95% CI 1.12-1.37), and those with no insurance (ARR = 1.75, 95% CI 1.63, 1.84).

Conclusions: Continuation was greatest in patients who were accessing PrEP with no medication copay, which supports increasing access to free or low-cost PrEP to maximize PrEP's

effectiveness at reducing HIV transmission in community settings. Efforts to support PrEP continuation among young people are warranted.

3.2 Background

Since tenofovir/emtricitabine (TDF/FTC) was approved for use as oral daily HIV pre-exposure prophylaxis (PrEP) by the Food and Drug Administration (FDA) in 2012, evaluation of PrEP use in United States community clinics has been ongoing.[1] Clinical trials have shown PrEP to be over 90% efficacious when taken consistently.[2] The Centers for Disease Control and Prevention (CDC) published guidelines on prescribing PrEP to people with HIV positive partners, men who have sex with men (MSM) with a six-month history of condomless anal intercourse or sexually transmitted infection (STI), and transgender women who have sex with cisgender (non-transgender) men.[3] The CDC recommends clinicians who prescribe PrEP have patients return for follow-up appointments at three-month intervals.[3]

Since PrEP is a relatively new tool in HIV prevention, measures of success are still being developed as patient use patterns are evaluated. The limited published studies on PrEP continuation have consistently found 30% or more of patients were not retained after three months.[4,5] Reasons for PrEP discontinuation described in the qualitative literature include structural (insurance, costs and copayments), social (stigma and relationship status), behavioral (sexual risk) and clinical factors (actual or perceived side effects).[6] Racial/ethnic disparities in PrEP discontinuation have also been documented.[7] To our knowledge, the degree to which these factors impact risk of discontinuation has not been established. As PrEP has become available in community settings, prevention care cascades have been proposed to evaluate its success as an HIV prevention strategy.[8,9] The measure of a successful PrEP intervention is not typically

lifelong adherence and may instead be PrEP use during "seasons of risk".[10,11] Determining the respective proportions of patients who discontinue PrEP due to access barriers versus reduction in HIV risk is crucial to allocating resources to support those who want to stay on PrEP.

In the United States, the cost of a PrEP prescription varies substantially by insurance status. As of 2016, a 30-day supply of TDF/FTC (available as brand name Truvada) was approximately $1,250 without insurance, not including the cost of medical care.[12] Gilead, the manufacturer of Truvada, has a patient assistance program that provides participants up to $3,600 annually in copay assistance. Insured and uninsured patients may apply for this copay card. TDF/FTC for PrEP is covered by all health insurance plans sold on Covered California, the state health insurance exchange set up by the Patient Protection and Affordable Care Act (ACA). A 2016 cost analysis of Covered California plans available in Los Angeles found that an individual may expect to pay approximately $50 per month for PrEP medication on a Gold or Silver plan (or $0 with the manufacturer's copay card), while those on a high-deductible Bronze plan may pay $500 per month (reduced to $200 per month with the copay card).[12] Individuals enrolled in Medi-Cal, California's Medicaid which was expanded through the ACA, have no copay for PrEP medication. In Los Angeles County, the Los Angeles Department of Public Health Division of HIV and STD Prevention (DHSP) PrEP program provides PrEP with no copay to eligible individuals who are uninsured or underinsured and did not qualify for Medi-Cal.

The aims of this analysis were three-fold: 1) characterize engagement in PrEP services in a community clinic, 2) identify demographic and health services correlates of PrEP discontinuation, 3) compare risk of HIV seroconversion among active and discontinued clients.

Understanding patterns of PrEP use in community settings can provide insight to maximize PrEP's contribution to HIV prevention.

3.3 Methods

This longitudinal analysis was conducted using electronic medical record data from the Los Angeles LGBT Center (the Center), a Federally Qualified Health Center in Los Angeles County. The Center started providing PrEP in 2014 through its primary care clinic in Hollywood, and expanded PrEP services in October 2015 to its sexual health clinic in West Hollywood. The Center accepted most health insurance plans, provided insurance benefits navigation, and offers primary care services to uninsured patients through a sliding scale fee system based on income. Clinic-based PrEP navigators helped PrEP patients enroll in Medi-Cal, apply for a copay card, and/or enroll in the DHSP PrEP program.

Patients seeking PrEP had an initial appointment with a medical care provider (physician, nurse practitioner, or physician assistant) for HIV testing and other laboratory tests recommended by the CDC. HIV testing included a rapid antibody test (results available within 30 minutes) and a quantitative RNA test (results available within 7-10 days). Patients who tested antibody positive via rapid HIV test received counseling and linkage to HIV treatment. Patients who tested antibody-negative via rapid test were provided an initial PrEP prescription, which could be filled at the Center's in-house pharmacy or another pharmacy. Patients whose rapid result was negative and RNA result was positive (consistent with acute HIV infection) were contacted immediately to discontinue PrEP and link to HIV treatment. The Center required PrEP patients to have an in-person visit with a provider after 30 days to refill the first prescription, repeat HIV testing, monitor laboratory values and side effects, and address adherence concerns. After the first follow-up appointment, three-month prescriptions were routinely provided, and

patients were instructed to return for quarterly monitoring appointments with a provider to continue receiving PrEP.

Medical records were abstracted for patients 18 and older prescribed TDF/FTC as PrEP at either of the Center's clinics between March 1, 2014 and March 1, 2017. Demographic variables –including age, gender, race/ethnicity, sexual orientation, housing status, education level, and location of residence – and clinical variables including laboratory results, visit dates, clinic locations, prescriptions, and insurance information were obtained from the Electronic Medical Record (EMR). Distance to clinic from patient's home address was calculated using the Google Maps Application Programming Interface in the R package ggplot. Insurance was categorized as Medi-Cal, DHSP, private (including employer-provided insurance and insurance purchased through Covered California), and none (uninsured/out of pocket).

Patient records entered the analysis from the day of first PrEP medical visit and were followed through September 10, 2017. HIV testing data were available through March 15, 2018. Because documentation of PrEP appointments evolved as the Center's program expanded, PrEP appointments during the analysis period were identified based on a combination of indicators in the EMR. Appointments were counted as PrEP visits if one or more of the following criteria were met: 1) Type of visit was recorded as PrEP Intake or PrEP Follow-up, 2) a prescription was ordered for "Truvada PrEP", 3) a prescription was ordered for "Truvada" and the visit was not recorded as an encounter for PEP. Non-PrEP visits met one of the following conditions: 1) no Truvada was prescribed, 2) type of visit was PEP Intake or PEP Follow-up, 3) "Truvada (PEP)" was prescribed. For patients whose first PrEP visit was not billed as PrEP Intake, charts were reviewed to verify start date. The primary outcome was PrEP status at the end of the analysis period: active, discontinued, or lost to follow-up.

Definitions

Active: Patient was prescribed TDF/FTC at the Center within the past 120 days.

Discontinued: Patient was most recently prescribed TDF/FTC at the Center more than 120 days ago, and has had at least one medical visit since receiving last PrEP prescription.

Lost to Follow-up: Patient was most recently prescribed TDF/FTC at the Center more than 120 days ago, and has had no medical visits since receiving last PrEP prescription.

Seroconversion: Development of HIV antibodies, detectable in blood, after exposure to HIV. Measured as date of first HIV positive test result.

Conceptual Model

A conceptual model of PrEP continuation (**Figure 1**) posits that to continue returning for PrEP appointments, patients need to be able to access and pay for PrEP, tolerate PrEP, and have a continued need for PrEP. Tolerating PrEP includes factors like no serious side effects, no contraindications, and being willing and able to take a daily pill. Besides accessing and tolerating PrEP, continued need for PrEP or motivation to use PrEP are essential to ongoing use. An individual's need for PrEP may end due to seroconversion, reduced HIV risk due to behavior or partnership factors, or adoption of other HIV prevention methods.

Statistical Methods

Risk of seroconversion, excluding those who tested positive on the day of first PrEP appointment, by status (active versus discontinued at time of seroconversion) was calculated and compared using a one-tailed Fisher's exact test. Patients who were lost to follow-up were not included in the calculation of HIV seroconversion risk. If patients seroconverted during active

PrEP status, their charts were reviewed to assess reported adherence to PrEP in the time leading up to the diagnosis. Differences in PrEP status by baseline characteristics were assessed using chi square tests (alpha = 0.05). A multivariable multinomial logistic regression model of PrEP status was then specified. Variables with large p-values (>0.1) in chi-square tests were not included in the multivariable model. For the multivariable model, reference groups were those with the greatest proportion active, except when category was less than 10% of sample, in which case the reference group was the category with greatest proportion active that included at least 10% of the sample. Resulting odds ratios were converted to risk ratios. While a small number of cisgender women (n=14), transgender men (n=11), genderqueer people (n=14) were prescribed PrEP at the Center during the analysis period, analyses were limited to cisgender men and transgender women due to small sample sizes of other genders. All analyses were performed using SAS 9.4 (Cary, N.C.).

Ethics

The study was approved by the Institutional Review Board at the University of California, Los Angeles (IRB#17-000717).

3.4 Results

The EMR records included 1,715 unique patients who initiated PrEP services at the Center. The sample included 1,646 cisgender men and 67 transgender women. Half were over 30 (age range 18 - 71); White (44%), Hispanic (30%), or Black (8%); and had sexual orientation of gay (83%) or bisexual (10%). Ten percent received PrEP through the Los Angeles County DHSP program, 35% had Medicaid, and 40% used private insurance. Just over half initiated PrEP at the Center's Hollywood location, and the majority lived within 10 miles of the clinic where they started PrEP (median = 5.7 miles, interquartile range= 2.1-10.9 miles) (**Table 1**). Demographic

characteristics differed significantly by site of first PrEP visit. Compared to those initiating at the West Hollywood location, those who started PrEP at the Hollywood clinic differed significantly by gender, age group, and sexual orientation.

At the end of the analysis period, 47% (n = 809) of patients who started PrEP were active – that is, had attended a PrEP appointment within the previous 120 days. Thirty-seven percent (n=633) had discontinued receiving PrEP, and 16% (n=273) were lost to follow-up.

Eleven patients who had a PrEP intake appointment were diagnosed with HIV during or after their first PrEP visit (**Figure 2**). Three tested HIV positive at their first PrEP appointment and were linked to HIV care. Six had discontinued PrEP before time of diagnosis (range: 169 – 424 days since last PrEP prescription). Two were active PrEP clients at time of HIV diagnosis. One patient tested positive for acute HIV infection at the first PrEP follow-up appointment, 48 days after PrEP was first prescribed. This timeline is consistent with infection prior to starting PrEP. Another patient tested positive for acute HIV infection at a PrEP follow-up appointment 104 days after most recent PrEP prescription. The medical chart for this patient was reviewed. At the visit, the patient had reported missing seven or more doses in a row. Overall incidence of seroconversion (excluding those who tested positive at baseline) was 0.76% (11 out of 1,442 not lost to follow-up). HIV risk in the discontinued group was significantly higher (one-tailed Fisher's exact test, p = 0.01) at 1.4% (n=9 of 633), compared to 0.25% (n=2 of 809) in the active group.

PrEP status differed significantly by age group, sexual orientation, type of insurance, clinic where patient received initial PrEP prescription, and year started PrEP but not by gender, race/ethnicity, housing status, education level, or distance between residence and clinic (**Table**

2). Sixty-one percent (n=99) of those who received PrEP through the DHSP PrEP program and 59% (n=349) of those on Medicaid were active at the end of the analysis period, compared to 44% (n=302) using private insurance and 19% (n=39) of uninsured patients.

After adjusting for all variables that had bivariate associations with PrEP status, age group, insurance type, and year of PrEP start remained significantly associated with risk of discontinuation in the multivariable model (**Table 3**). Compared to those aged 41-50, risk of discontinuation was significantly increased among younger people. Notably, those aged 18-24 had 41% greater (95% CI, 21%-57%) risk of discontinuation while those aged 25-30 appeared to have a slightly increased risk of discontinuation compared to older patients (ARR=18%, 95% CI, -2%, 36%). Compared to those on Medicaid, risk of discontinuation was 75% greater (95% CI, 63%-84%) among uninsured patients and 25% greater (95% CI, 12%-37%) among those with private insurance. Risk of loss to follow-up was 72% greater (95% CI, 55%-83%) among uninsured patients and 36% greater (95% CI, 19%-50%) among those using private insurance. Starting PrEP in 2016 – but not earlier – was significantly associated with increased risk of discontinuation and increased risk of loss to follow up compared to those who started in 2017.

3.5 Discussion

This longitudinal study of PrEP delivery at a community clinic with a broad age range and diverse population provides important data about PrEP delivery outside of clinical trial contexts. Eight new HIV diagnoses among over 1,400 patients (0.6%) who started PrEP over a three-year period demonstrates that PrEP is not only efficacious but also effective. By comparison, between 2014 and 2017, the annual incidence of HIV among patients testing at the Center declined from 2.8% to 1.3%. That six of eight new diagnoses among PrEP patients occurred among 663 patients who had discontinued PrEP (0.95%), compared to two among the

809 active patients (0.25%) is encouraging. Of the two infections diagnosed among active PrEP patients, one likely resulted from exposure to HIV before PrEP initiation, and one was diagnosed following a period of self-reported non-adherence. The two cases that arose among patients who were engaged with the PrEP program at the time of diagnosis underscore the need for early confirmation of HIV negative status to rule out acute infection, and the importance of adherence support.

The differential risk of seroconversion by PrEP status (active vs. discontinued) suggests that efforts to improve retention in PrEP programs will be key to reducing HIV transmission. Of note, only half of patients who had been prescribed PrEP were actively receiving PrEP at the end of the analysis period. The findings that risk of discontinuation was increased among younger people and decreased among those receiving PrEP through local and state government-funded programs have important implications for management of PrEP at the community level.

Because both the Los Angeles County DHSP program and Medi-Cal provide PrEP without a prescription copay, patients on these plans could pay substantially less than patients with other types of insurance, depending on their specific plan and utilization of the manufacturer's patient assistance program. That patients with lower cost to PrEP have better retention is consistent with qualitative findings that cite lack of health insurance and cost of medication as barriers to PrEP initiation and continuation. This finding supports increased allocation of resources to programs that provide consistent, low cost PrEP services. In addition to reducing the risk of HIV infection, initiating PrEP is an opportunity for linkage to primary care. Insurance benefit navigation that happens in the context of PrEP may therefore also enable patients to receive other health services.

Increased risk of discontinuation among those aged 18-24 is concerning given the elevated HIV incidence and reduced PrEP uptake observed in this age group.[13,14] Coupled with declining levels of PrEP adherence observed in the Adolescent Trials Network (ATN) 110 cohort, this reinforces the need for targeted strategies to meet the needs of young PrEP users. In the ATN 110 cohort, participants' main reasons for non-adherence included forgetting to take the pills (29%), being away from home (27%), or being too busy to take the pills (27%).[14] Less common reasons included avoiding side effects (4.5%), not wanting others to see them taking the pills (2.5%), or belief that the pill was harmful (2%).[14] These factors may influence attendance at PrEP appointments along with medication adherence, and strategies such as discreet reminders between appointments, continued education on how PrEP works, and flexible scheduling may simultaneously address adherence and retention challenges. Future studies should examine these and other potential barriers for younger PrEP users.

The finding that individuals who started PrEP in 2016 were most likely to discontinue PrEP may reflect an early-adopter effect. If those who started earlier in its availability in community settings were most motivated to use PrEP, they may also be more motivated to continue using PrEP for longer. Conversely, if PrEP's increasing availability led more patients who may be ambivalent candidates to try PrEP, a higher risk of discontinuation may reflect lower than anticipated personal need for PrEP or lower tolerance for drawbacks associated with PrEP. Future studies with reasons for PrEP discontinuation can illuminate the contributions of access barriers versus personal decision-making to PrEP discontinuation.

Strengths

The study had several key strengths, including longitudinal design, substantial sample size in a community-based sample, and ability to assess a variety of factors potentially relevant to PrEP discontinuation. A longitudinal design made it possible to assess risk of HIV infection, risk of discontinuation, and risk of loss to follow-up. By following all patients for at least six months, and some for as long as three years, we analyzed PrEP status over a longer term than has been typically available in early studies of PrEP discontinuation. The use of clinical care data from a sample of patients receiving PrEP in a primary care and sexual health setting may render findings more generalizable to other clinical settings where patients start PrEP outside of research studies. Using medical records data addressed generalizability problems inherent in clinical research where selected participants may not be representative of the broader patient population. Finally, the inclusion of detailed health insurance information, geographic distance, and demographic factors locally associated with increased HIV incidence enabled us to assessed stable personal factors and clinical factors on which a health system may be able to intervene.

Limitations

Use of the electronic medical record and a community-based sample brought strengths, but also introduced some limitations. Chiefly, it was not possible to determine the specific reasons people stopped coming to the Center for PrEP. Our clinical data did not contain information on changed HIV risk or "seasons of risk" that could lead to PrEP discontinuation – for example, a monogamous relationship with an HIV-negative partner, a period of sexual abstinence, or increased condom use [6, 10, 11]. Collecting this data in future studies will be crucial to know how to best support PrEP use as part of comprehensive HIV prevention. Furthermore, we could not distinguish between those who stopped using PrEP entirely and those who changed to a different provider. Because continuous attendance at PrEP appointments

depended on insurance status, we expect that some of those who stopped getting PrEP at the Center may have found a cheaper or more convenient way to obtain PrEP. through new insurance or a different provider. Additionally, HIV incidence in the discontinued group may be underestimated if some patients who discontinued PrEP did not later return to the Center for HIV testing. Furthermore, it was not possible to assess HIV incidence in the lost to follow-up group. Because data on PrEP adherence was not available, we could not precisely estimate the degree to which returning for PrEP appointments reflected ongoing PrEP use.

Other limitations related to individual variables may have influenced the ability to detect associations between certain factors and PrEP status. Ability to pay for PrEP may be determined by not only health insurance but also broader socioeconomic situation. In the present analysis, demographics, housing status, education level, and geographic location were used as proxies for socioeconomic status. Income and employment were not available, and many patients were missing education data. Socioeconomic status may therefore have been incompletely or inconsistently assessed. Similarly, without information about mode of transportation, distance from residence to clinic in miles is not necessarily informative. This is particularly relevant in Los Angeles, where public transit coverage and traffic pattern vary considerably within even narrow mileage categories, such that a five-mile distance could represent under ten minutes of travel time by car in non-rush hour traffic or longer than one hour via public transit.

Conclusions

Findings from this study indicate a relationship between robust insurance coverage for PrEP and long-term PrEP use. Increased risk of discontinuation among younger people suggests a need for continued efforts to provide biomedical HIV prevention services for youth. Future

studies qualitative who PrEP determine fraction of and proportion another

Table 3.1 Characteristics of cisgender men and transgender women receiving PrEP at the Los Angeles LGBT Center, n=1,715, starting between March 1, 2014 and February 28, 2017

	n	%
Gender		
Cisgender men	1646	96%
Transgender women	67	4%
Age group		
18-24	282	16%
25-30	570	33%
31-40	563	33%
41-50	210	12%
51-71	90	5%
Sexual Orientation		
Gay	1432	83%
Bisexual	169	10%
Other	67	4%
Unknown	47	3%
Race/Ethnicity		
Asian/Pacific Islander	117	7%
Black or African American	144	8%
Hispanic/Latino	521	30%
Other	110	6%
White	747	44%
Unknown	76	4%
Type of insurance		
Medicaid	595	35%
LA County DHSP	179	10%
Private	693	40%
None/out of pocket	195	11%
Unknown	53	3%
Clinic		
Hollywood	911	53%
West Hollywood	781	46%
Unknown	23	1%
Distance from clinic (miles)		
<1	217	13%
1 to < 5	552	32%
5 to <10	426	25%
10 to <20	286	17%
20 to <30	100	6%
30+	97	6%
Unknown	37	2%
Housing status		
Homeless	168	10%
Not homeless	1395	81%
Unknown	152	9%
Education level		
Less than college degree	732	43%
College degree or more	469	27%
Unknown	514	30%
Year started PrEP		
2014	39	2%
2015	325	19%
2016	1082	63%
2017	269	16%
Total	1715	100%

should collect data from patients stopped attending appointments to the attributable reasons for discontinuation identify the who transferred to provider.

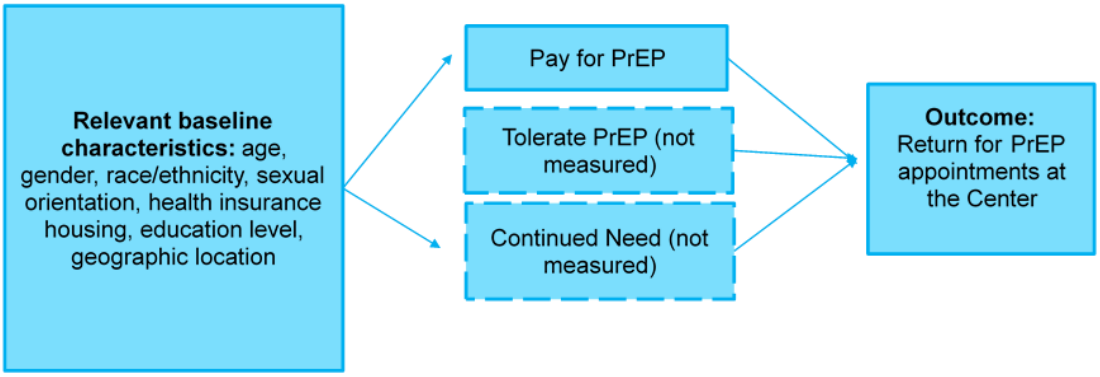
Table 3.2 Chi-square tests for differences in PrEP status at end of study by baseline characteristics of cisgender men and transgender women receiving PrEP at the Los Angeles LGBT Center, n=1,715, starting between March 1, 2014 and February 28, 2017

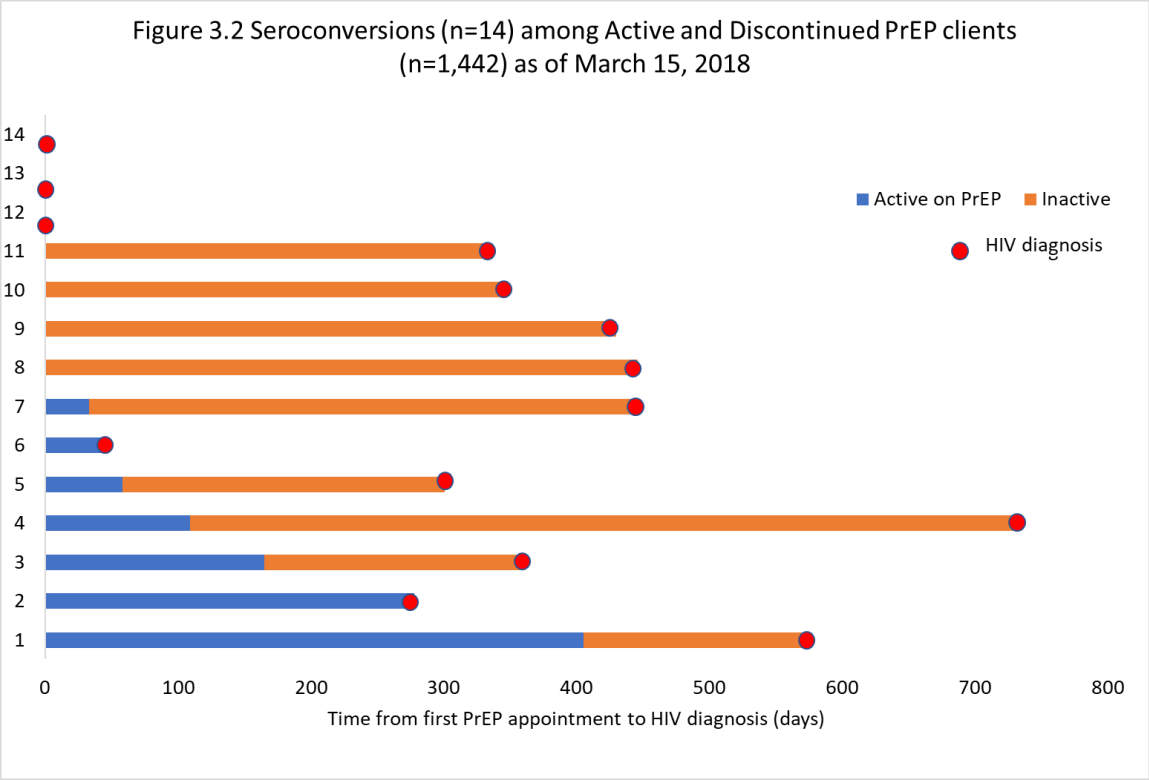
	Total		Active		Discontinued		Lost to Follow Up		
	n	%	n	%	n	%	n	%	p-value
Gender									0.06
Cisgender men	1648	96%	781	97%	600	95%	267	98%	
Transgender women	67	4%	28	3%	33	5%	6	2%	
Age group									0.0009
18-24	282	16%	108	13%	134	21%	40	15%	
25-30	570	33%	260	32%	218	34%	92	34%	
31-40	563	33%	273	34%	193	30%	97	36%	
41-50	210	12%	117	14%	63	10%	30	11%	
51-71	90	5%	51	6%	25	4%	14	5%	
Sexual Orientation									0.007
Gay	1437	84%	682	84%	507	80%	243	89%	
Bisexual	169	10%	71	9%	79	12%	19	7%	
Other	67	4%	31	4%	31	5%	5	2%	
Race/Ethnicity				0%					0.9
Asian/Pacific Islander	117	7%	52	6%	42	7%	23	8%	
Black or African American	144	8%	65	8%	54	9%	25	9%	
Hispanic/Latino	521	30%	236	29%	204	32%	81	30%	
Other	116	7%	55	7%	38	6%	17	6%	
White	747	44%	362	45%	266	42%	119	44%	
Type of insurance									<0.0001
Medicaid	595	35%	356	44%	175	28%	64	23%	
LA County DHSP	179	10%	115	14%	35	6%	29	11%	
Private	693	40%	308	38%	254	40%	131	48%	
None/out of pocket	195	11%	29	4%	126	20%	40	15%	
Clinic									<0.0001
Hollywood	911	53%	487	60%	295	47%	129	47%	
West Hollywood	781	46%	312	39%	329	52%	140	51%	
Distance from clinic (miles)									0.1
<1	217	13%	99	12%	88	14%	30	11%	
1 to < 5	552	32%	284	35%	189	30%	79	29%	
5 to <10	426	25%	190	23%	164	26%	72	26%	
10 to <20	286	17%	143	18%	100	16%	43	16%	
20 to <30	100	6%	42	5%	37	6%	21	8%	
30+	97	6%	34	4%	42	7%	21	8%	
Housing status									0.19
Homeless	168	10%	76	9%	73	12%	19	7%	
Not homeless	1395	81%	669	83%	516	82%	210	77%	
Education level									0.16
Less than college degree	469	27%	203	25%	202	32%	64	23%	
College degree or more	732	43%	343	42%	275	43%	114	42%	
Year started PrEP									<0.0001
2014	39	2%	28	3%	9	1%	2	1%	
2015	325	19%	171	21%	109	17%	45	16%	
2016	1082	63%	451	56%	446	70%	185	68%	
2017	269	16%	159	20%	69	11%	41	15%	
Total	1715	100%	809	100%	633	100%	273	100%	

Table 3.3 Adjusted risk ratios for PrEP discontinuation and loss to follow-up among cisgender men and transgender women, n=1,715, starting PrEP at the Los Angeles LGBT Center between March 1, 2014 and February 28, 2017

	Discontinued		Lost to follow up	
	Adj Risk Ratio	95% CI	Adj Risk Ratio	95% CI
Gender				
Cisgender men (ref)	1.00	--	1.00	--
Transgender women	1.15	(0.79, 1.47)	0.92	(0.44, 1.45)
Age group				
18-24	**1.41**	**(1.21, 1.57)**	1.19	(0.91, 1.45)
25-30	1.18	(0.98, 1.36)	1.14	(0.89, 1.37)
31-40	1.13	(0.93, 1.31)	1.15	(0.91, 1.38)
41-50 (ref)	1.00	--	1.00	--
51-71	0.98	(0.69, 1.28)	1.02	(0.65, 1.39)
Sexual Orientation				
Gay (ref)	1.00	--	1.00	--
Bisexual	1.17	(0.99, 1.35)	0.86	(0.61, 1.14)
Other	1.10	(0.77, 1.41)	0.77	(0.35, 1.30)
Type of insurance				
Medicaid (ref)	1.00	--	1.00	--
LA County DHSP	0.78	(0.57, 1.01)	1.11	(0.85, 1.37)
Private	**1.25**	**(1.12, 1.37)**	**1.36**	**(1.19, 1.50)**
None/out of pocket	**1.75**	**(1.63, 1.84)**	**1.72**	**(1.55, 1.83)**
Clinic				
Hollywood (ref)	1.00	--	1.00	--
West Hollywood	1.12	(0.99, 1.24)	1.10	(0.95, 1.26)
Year started PrEP				
2014	1.03	(0.62, 1.43)	0.62	(0.18, 1.34)
2015	1.21	(0.99, 1.40)	1.12	(0.85, 1.37)
2016	**1.35**	**(1.18, 1.49)**	**1.25**	**(1.04, 1.44)**
2017 (ref)	1.00	--	1.00	--

Figure 3.1 Conceptual model of PrEP Continuation





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Chapter 4. Joint Trajectories of Methamphetamine Use and HIV Treatment Outcomes in a Cohort of Men of Color Who Have Sex with Men

4.1 Abstract

Background: Methamphetamine is highly addictive, interfering with adherence to HIV treatment and care. To identify effects of use patterns, we characterized the trajectories of methamphetamine use (including self-reported frequency and urine drug screen) and HIV viral load (HVL) over 18 months in a cohort of HIV positive men of color who have sex with men (MoCSM) aged 18-45. We hypothesized that longitudinal patterns of frequent or recent methamphetamine use would be associated with longitudinal patterns of viremia.

Methods: The study included 151 HIV-positive men who enrolled in the NIDA-funded mSTUDY cohort between August 2014 and July 31, 2016. Methamphetamine use and HVL were assessed at baseline and visits every six months. Methamphetamine use was assessed via computer-assisted self-interview and urine drug screen. HVL was assessed via polymerase chain reaction. Group-based trajectory models (GBTMs) were constructed using censored normal distributions to model trajectories of methamphetamine frequency and log viral load, and a binomial distribution to model trajectories of toxicology results. A joint trajectory model was specified to determine conditional probabilities of viremia trajectory given methamphetamine toxicology trajectory.

Results: GBTMs identified three methamphetamine toxicology trajectory groups: 1) negative (64% of participants), 2) dynamic (23%), and 3) positive (13%). Four HVL trajectory groups were identified: 1) undetectable (49%), 2) rising (13%), declining (18%), and high (19%). Conditional probability of high HVL given positive toxicology was 52% (95% CI 26%, 78%) compared to compared to 8% (95% CI 0%, 17%) given negative toxicology. Those who never

tested positive for recent methamphetamine use were most likely to have a consistently undetectable HVL (64%, 95% CI: 51%, 77%).

Conclusion: Frequent methamphetamine use over time was associated with a longitudinal pattern of viremia. To improve treatment outcomes for those living with HIV, frequency of use of substances such as methamphetamine needs to be addressed.

4.2 Background

Methamphetamine use is associated with HIV acquisition, disease progression, and reduced adherence to treatment among men who have sex with men (MSM).[1–4] Relationships between longitudinal patterns of substance use, including methamphetamine, and changes in HIV risk behaviors have been demonstrated in two large cohort studies.[5,6]

An analysis of stimulant (including methamphetamine) use trajectories among MSM in the Multicenter AIDS Cohort Study (MACS) identified four distinct trajectories.[5] Compared to the no use trajectory, those on an increasing trajectory reported having condomless receptive anal sex with a significantly greater number of partners. Those whose stimulant use decreased over time had a significant reduction in condomless receptive anal sex partners compared to those who consistent reported no use.[5] Colfax et al analyzed how individuals' sexual risk behavior changed in relation to frequency of methamphetamine, cocaine, or popper (amyl nitrite) use.[6] Compared to periods of no drug use, both light (less than weekly) and heavier (weekly or more) drug use periods were associated with increased odds of having condomless anal intercourse with a partner of unknown HIV status.[6]

Though longitudinal relationships between stimulant use and HIV risk behaviors have been documented, most studies on the relationship between methamphetamine and HIV treatment outcomes have focused on recent methamphetamine use rather than longitudinal patterns. Beyond affecting HIV risk behaviors, recent methamphetamine use has been shown to influence treatment outcomes in HIV positive MSM. Some *in vitro* evidence and evidence from mouse models suggests that methamphetamine administration increases HIV replication; however, epidemiological does not support a direct effect of methamphetamine on viral load.[7] Recent stimulant use was associated with lower adherence to HAART as measured by a medication events monitoring system (MEMS).[8] Among patients on HAART, those who tested positive for methamphetamine on urine drug screen had higher viral loads compared to patients who tested negative for recent methamphetamine use.[3] Because viral load among patients not on HAART did not significantly differ by methamphetamine toxicology, these results did not support a direct effect of methamphetamine on viral load.[3] Rather, this difference may be due to poorer adherence, and not an interaction between methamphetamine and antiretrovirals.

In the United States, young Black or African American, Hispanic or Latino, and other men of color who have sex with men (MoCSM) have higher rates of HIV despite reporting similar risk behaviors to White MSM.[9–12] Previous analyses of stimulant use trajectories were conducted in cohorts of predominantly older and White MSM.[5] Disparities in HIV care for Black and Hispanic/Latino MoCSM have also been documented.[10,13] Examining the relationship between methamphetamine use and HIV outcomes in a cohort of young MoCSM can thus be valuable to developing targeted strategies to end the epidemic.

The objective of this study was to determine whether longitudinal patterns of frequent or recent methamphetamine use were associated with poorer HIV treatment outcomes. The study aims to 1) characterize trajectories of methamphetamine use over a period of 18 months among young adult MSM of color who are HIV positive, 2) characterize trajectories of HIV viral load in the sample, 3) determine relationship between longitudinal pattern of methamphetamine use and HIV treatment outcomes. It was expected that a longitudinal pattern of frequent methamphetamine use would be associated with increased viral load and decreased CD4 count compared to consistent non-use of methamphetamine.

4.3 Methods

The mStudy (MSM and Substances Cohort at UCLA Linking Infections, Noting Effects) is a cohort of predominantly Black and Latino MSM aged 18-45 who are HIV positive or at high risk of HIV infection, with a focus on non-injection substance use. This analysis included HIV positive participants who enrolled in mStudy between September 2014 and July 2016. Participants were followed through the later of fourth visit or February 28, 2018. At the initial visit and follow up visits every six months, participants completed a computer-assisted structured interview (CASI), had urine drug screening, tested for sexually transmitted infections (STIs), and had HIV-related laboratory tests (CD4 count, viral load).

Measures

At each visit, participants reported methamphetamine use in the past six months as daily, weekly, monthly, less than monthly, once, or never. A urine drug screen was performed at each visit using CLIA waived radioimmune assay strips to test for methamphetamine and other drugs (other amphetamines, cocaine, ecstasy, marijuana, nitrites, opiates). The threshold for detecting

amphetamines was 300 ng/ml, and the screening was used to detect recent (past 3 days) use of methamphetamine and d-amphetamine, a methamphetamine metabolite. HIV RNA and CD4 levels were measured at each visit, and dichotomized. An undetectable viral load was <20 copies/mL, and a low CD4 count was <200. Baseline antiretroviral (ART) use was assessed by self-report of current prescription at the enrollment visit. The questions "Are you currently receiving treatment for substance use, including alcohol?" and "Are you currently participating in a 12-step program like AA, NA, CA?" were used to assess baseline substance use treatment and participation in a 12-step program, respectively.

Statistical methods

Descriptive statistics including frequency distributions for categorical variables and, mean and standard deviation for continuous variables were calculated. Differences between groups were evaluated using chi-square tests– and Fisher's exact tests or multinomial logistic regression when cell sizes were small – were performed to assess correlates of group membership, and differences in viral load and CD4 count at last visit between methamphetamine trajectory groups

Group-based trajectory models (GBTM) can identify a population's underlying groups that may follow different trends over time.[14–17] Standard growth curve modeling assumes a longitudinal outcome will follow a similar pattern between persons, and that differences in this pattern can be predicted by pre-specified within-person characteristics (e.g., age, gender, biomarkers).[14] On the other hand, GBTMs can be used to characterize the shape of trajectories without prior knowledge of what factors might affect group membership.[14]

GBTMs were constructed with SAS Proc Traj and methamphetamine use was modeled in two ways – with a binomial distribution to model trajectories of urine drug results, and a censored normal distribution to model trajectories of self-reported frequency. Log viral load trajectories were modeled with a censored normal distribution. For all models, model selection was performed in two stages, first determining number of groups to minimize Bayesian Information Criteria (BIC), and then determining the polynomial order of groups.[14] A zero-order group was included in all candidate methamphetamine models based on the expectation that some participants would have a negative drug screen at all visits and report no methamphetamine use throughout the study. A joint GBTM was then specified to estimate probabilities of viral load trajectory group membership conditional on methamphetamine use trajectory group membership. Model accuracy was assessed by calculating odds of correct classification (compared to random assignment, so higher odds denotes better accuracy and a threshold of 5 is conventionally used) based on average posterior probability of group membership (conventional threshold is > 0.70 for all groups).[14,18]

To examine the effect of methamphetamine initiation (or re-initiation) on HIV viral load, a post-hoc analysis of those who screened negative for methamphetamine at baseline was performed. We performed an analysis of variance (ANOVA) to compare viral load between those with a negative urine drug screen for methamphetamine at all visits to those who screened positive at one or more subsequent visits.

Chi-square tests – and Fisher's exact tests or logistic regression when cell sizes were small – were performed to assess correlates of group membership, and differences in viral load and CD4 count at last visit between methamphetamine trajectory groups. To examine the effect of methamphetamine initiation (or re-initiation) on HIV viral load, a post-hoc analysis of those

who screened negative for methamphetamine at baseline was performed. We performed an analysis of variance (ANOVA) to compare viral load between those who screened negative at all visits to those who screened positive at one or more subsequent visits. All analyses were performed in SAS 9.4 (Cary, N.C.).

Ethics

The study was approved by the Institutional Review Board at the University of California, Los Angeles (IRB #13-001749).

4.4 Results

From September 2014 to February 2018, 151 individuals contributed 512 visits. Participant mean and median age was 35 (standard deviation 6.5 years). Forty-two percent of participants identified as Hispanic or Latino, and 47% Black, Non-Hispanic (**Table 1**). For subsequent analyses, race/ethnicity was categorized as Hispanic, Black, or Other. At baseline visit, 40 participants (26%) had a positive urine drug screen for methamphetamine and d-amphetamine, indicating recent use. One additional participant screened positive for d-amphetamine but negative for methamphetamine, indicating previous use of methamphetamine or recent use of other amphetamine(s). Over half of participants (n=86) reported some level of methamphetamine use in the past six months. Twelve percent (n=18) reported daily use, 21% (n=32) reported weekly use, and 8% (n=11) reported monthly use. Seven percent (n=10) reported using methamphetamine once in the past six months, and 10% (n=15) reported using methamphetamine more than once but less than monthly. At baseline, 13% reported currently receiving substance use treatment (for methamphetamine or other substances) and 26% reported participating in a 12-step program. At baseline, 60% had detectable viral load (>20 copies/mL). Eleven percent (n=16) had a baseline CD4 count <200. Most participants had four visits in the

study period, with an average time between visits ranging from 179 to 196 days. Nineteen participants (13%) were missing their second visit, while 40 (26%) did not have a fourth visit by the end of the study period. Missing follow-up visits were not significantly associated with baseline methamphetamine toxicology, baseline methamphetamine self-reported use, age, or race/ethnicity.

Frequency of methamphetamine use

Using self-reported frequency of methamphetamine use in the past six months, five trajectories were identified – frequent use (4%), moderate use (37%), declining (12%), occasional (12%), and never (35%) (**Figure 1**). BIC was substantially improved in the 5-group model over the 3-group and 4-group models, despite the small sample size of some of the groups in the 5-group solution. Group membership did not significantly differ by age ($p=0.9$, multinomial logistic regression with continuous age) or race /ethnicity ($p=0.22$, chi-square) but did differ by baseline methamphetamine toxicology ($p<0.0001$). While baseline ART and baseline substance use treatment did not significantly differ between groups, participation in a 12-step program at baseline did differ between groups ($p=0.04$). About half of those in the declining and occasional use reported participating in a 12-step program at baseline, compared to about 20% of those in the other groups. Average posterior probability for each group ranged from 0.86 for the occasional group to 0.96 in the frequent use group. Odds of correct classification ranged from 24 for the moderate group to 516 for the frequent use group.

Biomarker of methamphetamine use

Using urine drug screen data, three methamphetamine use trajectories were identified – consistently negative (64%); consistently positive (13%); and dynamic, negative at some visits

and positive at others (23%) (**Figure 2**). Group membership did not differ by age (p=0.7, multinomial logistic regression with age as a continuous variable), race/ethnicity (p=0.6, multinomial logistic regression), or baseline ART use (p=0.25). Both substance use treatment (p=0.03) and participation in a 12-step group (p=0.01) predicted methamphetamine drug screen group membership. At baseline, 19% of those in the consistently negative group reported participating in substance use treatment (not necessarily for methamphetamine), compared to 4% of those in the dynamic group and none of those in the positive group. About a third of the negative group reported participating in a 12-step program at baseline, compared to 8% of those in the dynamic group and 17% of those in the positive group. Average posterior probability ranged from 0.80 for the consistently positive group to 0.91 for the consistently negative group. Odds of correct classification ranged from 5.7 in the consistently negative group to 25 in the consistently positive group.

Comparing biomarker and behavioral group assignments

Ninety-six percent (n= 54) of those assigned to the never use group in the frequency GBTM were in the negative group in the urine drug screen GBTM. Ninety-four percent (n=15) of those in the declining frequency group were assigned to the negative drug screen group. Most (81%, n=13) of those in the occasional use group of the GBTM were in the negative drug screen group, while the remaining 19% (n=3) were in the dynamic drug screen group. The moderate frequency group was split between the three drug screen groups, with 37% (n=21) in negative, 33% (n=19) in dynamic, and 29% (n=17) in positive. Most (67%, n=4) of those in the high frequency group were assigned to the positive drug screen group, with the remaining two in the dynamic group.

Log viral load

For modeling, an undetectable viral load was set to 19 copies/mL (log VL = 1.28). Four trajectory groups emerged– high (19%), rising (13%), declining (18%), and low/undetectable (49%) (**Figure 3**). Average posterior probability ranged from 0.83 in the high group to 0.94 in the low group. Odds of correct classification ranged from 15.7 (low group) to 80.5 (rising group). Viral load trajectory significantly differed by baseline ART use ($p<0.0001$). Fifty-seven percent of those in the low/undetectable group and 70% of those in the rising group reported using ART at baseline, compared to 21% of the high group and 24% of the declining group. Though baseline ART use did not differ by race/ethnicity or age, viral load trajectory was significantly different by race/ethnicity ($p=0.03$). Forty-two percent of Hispanic/Latino participants had consistently undetectable viral load, compared to 51% of Black participants and 76% of participants of another race/ethnicity. Nearly a third of Black participants (n=22) had consistently high viral load, compared to 17% (n=11) of Hispanic/Latino participants. Hispanic/Latino participants comprised the majority of both the rising and declining viral load trajectories with 11 members of each.

Joint Trajectories

Viral load trajectory differed based on methamphetamine urine drug screening results trajectory (**Figure 4**). Over half of those with consistently positive urine drug screens had a high viral load (52%, 95% confidence interval (CI): 26%, 78%) compared to 8% (95% CI 0%, 17%) of those with consistently negative urine drug screens. Probability of increasing viral load trajectory was similar between the never use group (17%, 95% CI: 7%, 27%) and the consistent use group (19%, 95% CI: 0%, 39%). About half of those in the dynamic group were in the

declining viral load trajectory (49%, 95% CI: 15%, 83%). Those who never tested positive for recent methamphetamine use were most likely to have a consistently undetectable viral load (probability=64%, 95% CI: 51%, 77%).

There was insufficient power to model joint trajectories of self-reported methamphetamine use and log viral load due to the number of groups in each single trajectory model. To assess the effect of frequency of methamphetamine use on HIV treatment outcomes, we compared between-group differences in binary HIV treatment outcomes. Overall, 45% (n=68) of participants had detectable viral load at the fourth visit (or last visit if fourth visit was missing), and 5% (n=8) had a CD4 count under 200. Risk of detectable viral load at last visit (p=0.03), and risk of low CD4 count at last visit (p=0.004) both differed significantly by trajectory group (**Table 2**). Of the six individuals classified in the frequent use group, all six had a detectable viral load at last visit, and three had a CD4 count under 200. About half of the moderate and occasional use groups had a detectable viral load at last visit.

Methamphetamine initiation

At baseline visit, 111 participants (74%) had negative drug screen for methamphetamine. The majority had negative screens at all subsequent visits, but 20 (18%) tested positive for recent methamphetamine use at one or more subsequent visit. Of the 20 whose urine drug screens patterns were consistent with "initiation," the self-report data were mixed. At baseline, five reported no use in the past six months, and five reported once or less than monthly. The remaining 10 reported daily (n=2), weekly (n=5), or monthly (n=3). Those who were negative at baseline and later screened positive for recent methamphetamine use were more likely to have a detectable viral load at last visit compared to those with a negative drug screen for

methamphetamine at all visits (60% versus 34%, p = 0.04). Neither age, race/ethnicity, CD4 count or log viral load at last visit differed significantly by methamphetamine initiation status. None of those who went on to initiate methamphetamine use were in substance use treatment at baseline, compared to 21% of those whose toxicology was negative at all visits.

4.5 Discussion

Distinct trajectories of methamphetamine use emerged in a cohort of HIV-positive men of color who have sex with men (MoCSM). With the biomarker measure of methamphetamine use (urine drug screen), we identified three trajectories that can be summarized as chronic use, intermittent use, and never use. Using a behavioral measure of methamphetamine use (self-reported use in the past six months), we identified five trajectories that broadly correspond to these three – frequent and moderate use, occasional and declining, or no use. Though some of the five groups are small in this sample, the additional behavioral data illustrates how different patterns of methamphetamine use may be captured with momentary toxicology. The two types of measures overlapped logically, with nearly all who were assigned to the trajectories for never use or decreasing use also having negative urine drugs screen across visits. That the moderate frequency group was split between the three drug screen trajectories is consistent patterns of methamphetamine use (weekly or monthly) that would be captured differently in an assessment that captures only recent use. For both types of measures, longitudinal patterns of recent or frequent methamphetamine use were associated with higher HIV viral load and lower CD4 counts over time.

Most men reported at least some methamphetamine use during the 18 months of follow-up. A small minority reported daily use throughout the study, but the majority who used methamphetamine reported using weekly or less often. Toxicology trajectories were consistent

with these patterns. The 16% who consistently screened positive for recent methamphetamine use were substantially more likely to have a pattern of high viral load than the 59% who consistently screened negative for recent methamphetamine use. Reporting substance use treatment or participation in a 12-step program at baseline was predictive of longitudinal methamphetamine trajectory, reinforcing the need for substance use treatment to be part of HIV care. Compared to those who screened negative at every visit, those who initiated methamphetamine use after screening negative at baseline were more likely to have detectable viral load at the end of the study period. The results suggest that while any methamphetamine use was associated with detectable viral load over time, different longitudinal patterns may have different implications for HIV treatment.

Similar to the stimulant use trends observed in the MACS and EXPLORE studies, we found that for most participants, self-reported methamphetamine use stayed relatively constant or decreased over time. Though no "increasing use" trajectory emerged in the self-reported analysis, the post-hoc analysis of toxicology data found that 13% (n=20) initiated (or reinitiated) methamphetamine use after having a negative urine drug screen at the first visit. This demonstrates one contribution that combining biomedical and behavioral data can have to understanding trends in substance use. The mStudy cohort differs from the MACS and EXPLORE cohort in a few key ways. Our cohort includes primarily MoCSM, and is among the first studies to examine the relationship between methamphetamine and viremia in this population. Additionally, the mStudy cohort is substantially younger than the MACS (where 6% were under 29 and 39% were 50 and over) and has a more similar but still younger age distribution to the EXPLORE [5,6]

By examining both behavioral and biomarker data, we assessed methamphetamine use more comprehensively than studies that use only one type of measure. Broadly, the two measures led to the similar conclusions – there appeared to be a dose response between methamphetamine use and probability of detectable viral load. With the frequency data that included daily use, we were able to raise the ceiling on the amount of use we could detect compared to the MACS, which used a binary measure of ever in the past six months, or EXPLORE, where the highest-use category was "weekly or more."[5,6] The trade-off in separating these groups is that some became very small. Because methamphetamine produces dependence in regular users, we expect that a larger sample would also yield a group who used daily. The presence of a declining group but not an increasing group in the GBTM could be an artifact of the small sample size, or it could indicate that individuals whose methamphetamine use was increasing were less likely to enroll in the study, similar to Project EXPLORE.[6] Though our sub-analysis was not adequately powered to assess differences in viral load magnitude following methamphetamine initiation, the finding that change from negative to positive urine drug screen during the follow-up period was associated with having a detectable viral load suggests future studies should examine this question in a larger sample.

Strengths

The study had several key strengths. The longitudinal design, study population, and combination of biomedical and behavioral data allowed us to investigate the relationship between methamphetamine and HIV treatment outcomes in a group most affected by HIV in the United States.[9] Using GBTMs enabled us to statistically assess model accuracy, which would not have been possible if we made the categorizations ourselves. High average posterior

probabilities, and high odds of correct classification compared to chance suggest the models accurately assigned participants to groups.

Limitations

Because the overall sample was relatively small, some of the frequency trajectories (e.g., daily use, declining) contained 12 or fewer participants. Repeating this analysis in a larger sample can elucidate whether these groups are stable in large sample sizes. Because no increasing group emerged, the relationship between methamphetamine and viremia observed in this study may not fully capture the effect of increasing methamphetamine use on viral load. Absence of an increasing group may be partially due to a ceiling effect – once a participant reached daily methamphetamine use in the frequency scale or positive in the urine drug screen, we could not capture further escalating patterns of use.

There was a fair amount of missing data, and though we investigated whether missingness was associated with demographics or baseline methamphetamine use, we could not rule out the possibility that missingness was dependent on another characteristic that we did not assess. GBTMs can accommodate data that is missing completely at random (that is, not dependent on any covariate). Though it is not possible to conclusively assess whether the GBTM's assumption that data were missing completely at random was met, we investigated whether this assumption was violated. We investigated whether demographics, baseline methamphetamine frequency, or baseline methamphetamine toxicology predicted missingness. The absence of significant associations between these variables and missingness did not prove the assumption was met; however, we proceeded with the analysis. If missingness was non-ignorable, or was dependent on another covariate, the trajectory group assignments may not be valid.

In conclusion, by considering both behavioral and biomedical measures of methamphetamine use, we found evidence of stable and distinct trajectories of methamphetamine use among MoCSM over an 18-month period. Additionally, we demonstrated that methamphetamine trajectories were associated longitudinally with key HIV treatment outcomes, including viremia and CD4 levels. That methamphetamine use, particularly methamphetamine addiction, are associated with worse HIV treatment outcomes is consistent with the existing literature. Our study identifies a link between methamphetamine use and viremia among MoCSM that, to our knowledge, has not been described in the literature. By linking patterns of consistent methamphetamine use (both in terms of recent and frequent use) to greater viremia, we reaffirmed the role of methamphetamine use and addiction as a disorganizing behavioral factor that adversely affects the health of MoCSM. Our findings reinforce the potential of substance use treatment to improve HIV treatment in a population with critical HIV disparities.

Table 4.1 Baseline characteristics of HIV positive men who have sex with men enrolled in mStudy before July 1, 2016, n=151

	n	%
Age		
18-24	12	8%
25-29	28	19%
30-34	37	25%
35-39	42	28%
40-45	32	21%
Hispanic, any race	64	42%
Non-Hispanic		
Black	71	47%
White	9	6%
More than one race	4	3%
Unknown race/ethnicity	3	4%
HIV Treatment Outcomes		
Current antiretroviral therapy	68	45%
Detectable viral load (>20 copies/mL)	90	60%
Low CD4 count (<200)	16	11%
Urine toxicology screen positive for any substance	80	53%
Methamphetamine Use: Urine tox screen positive	40	26%
Methamphetamine Use: Self-report, past 6 months		
Daily	18	12%
Weekly	32	21%
Monthly	11	7%
Less than monthly	15	10%
Once	10	7%
Never	63	42%
Currently receiving substance use treatment	20	13%
Participating in a 12-step program	39	26%
Total	151	100%

Table 4.2 Differences in HIV treatment outcomes at last visit by 18-month methamphetamine use trajectory, self-reported frequency, n=151

	Total	Detectable viral load (>20 copies/mL), p=0.01 [a]		CD4 count <200, p=0.004 [b]	
Methamphetamine Use Trajectory		n	%	n	%
Never	56	19	34%	1	2%
Declining	16	5	31%	1	6%
Occasional	16	9	56%	0	0%
Moderate	57	29	51%	3	5%
Frequent	6	6	100%	3	50%

a. Chi-square test b. Fisher's exact test

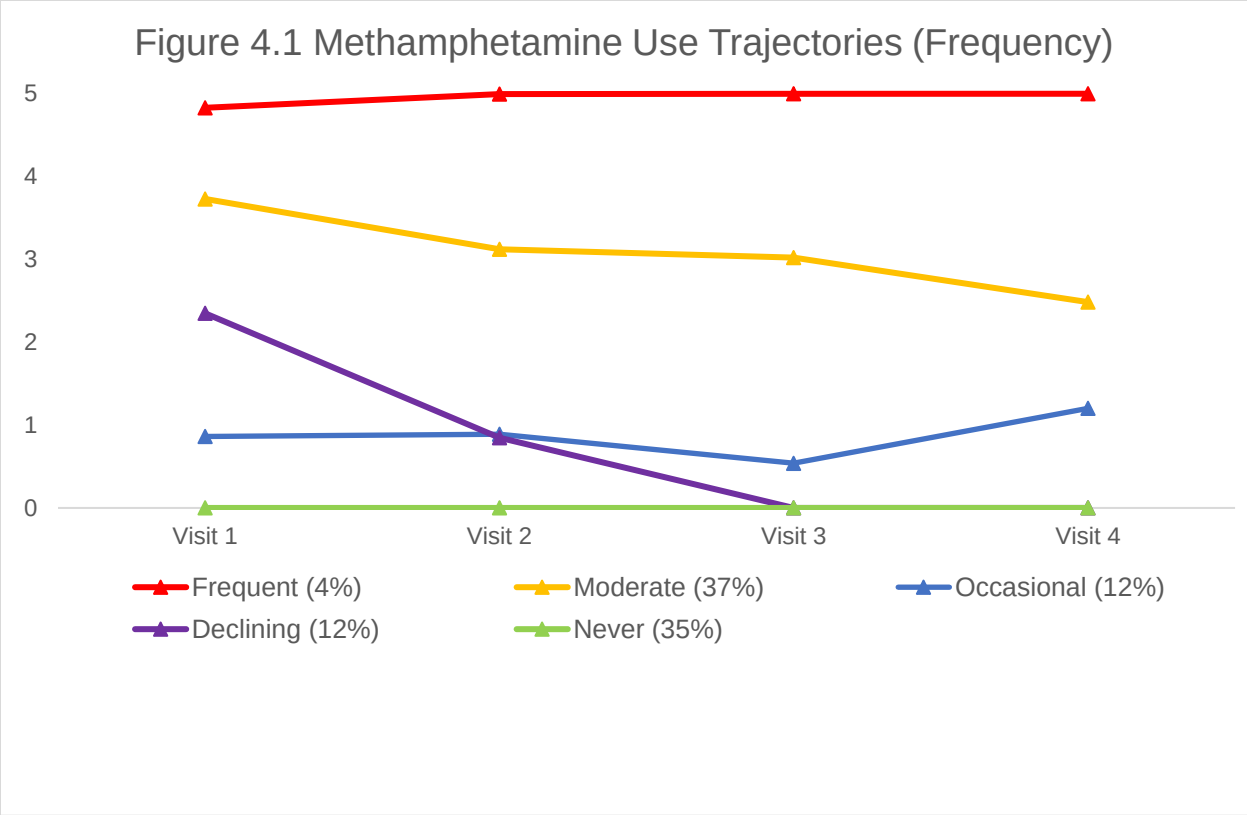
Figure 4.1 Methamphetamine Use Trajectories (Frequency)
5
4
3
2
1
0
Visit 1
Visit 2
Visit 3
Visit 4
Frequent (4%)
Moderate (37%)
Occasional (12%)
Declining (12%)
Never (35%)

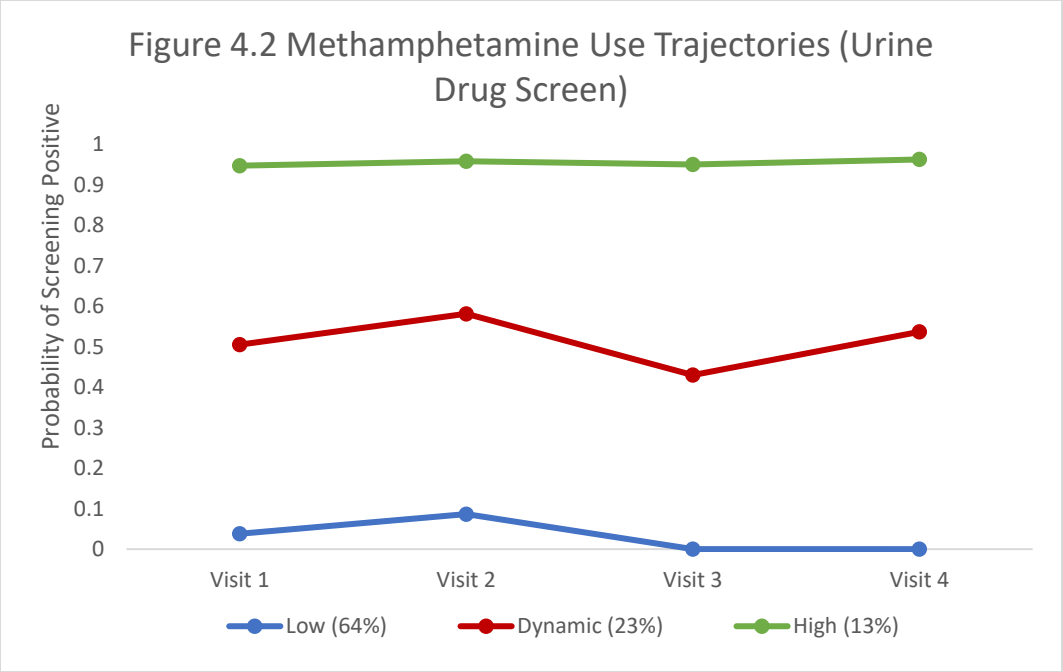
Figure 4.2 Methamphetamine Use Trajectories (Urine Drug Screen)
Probability of Screening Positive
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Visit 1
Visit 2
Visit 3
Visit 4
Low (64%)
Dynamic (23%)
High (13%)

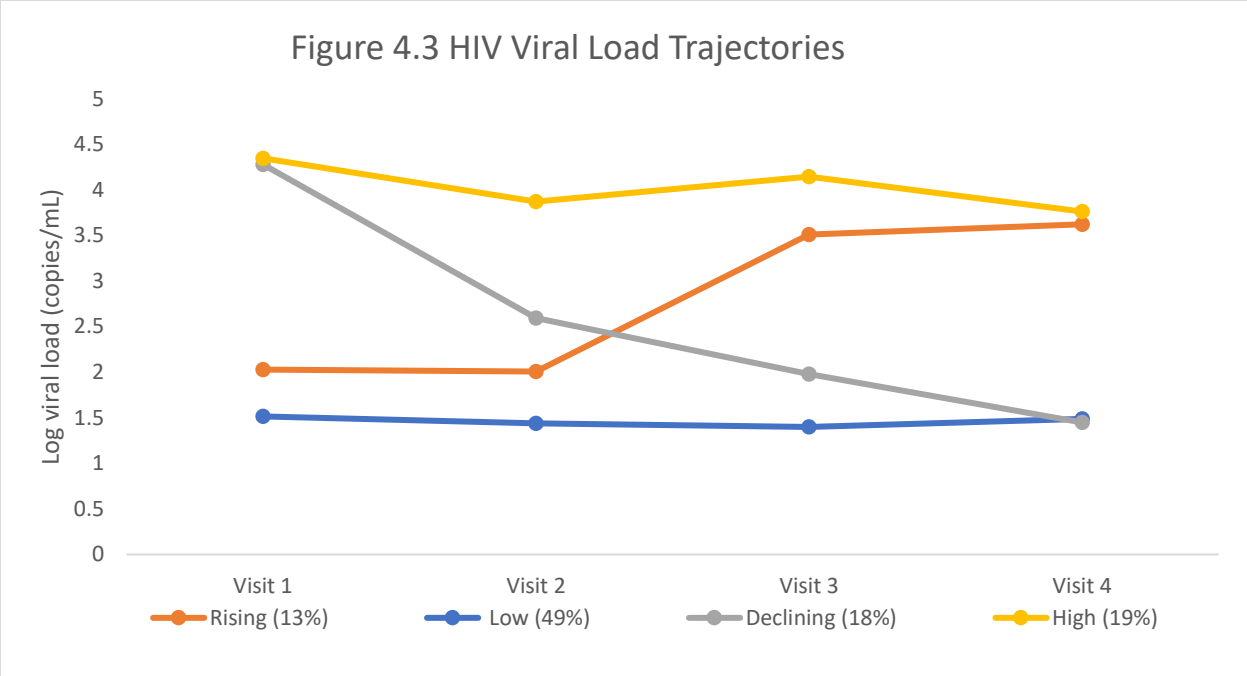
Figure 4.3 HIV Viral Load Trajectories
Log viral load (copies/mL)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Visit 1
Visit 2
Visit 3
Visit 4
Rising (13%)
Low (49%)
Declining (18%)
High (19%)

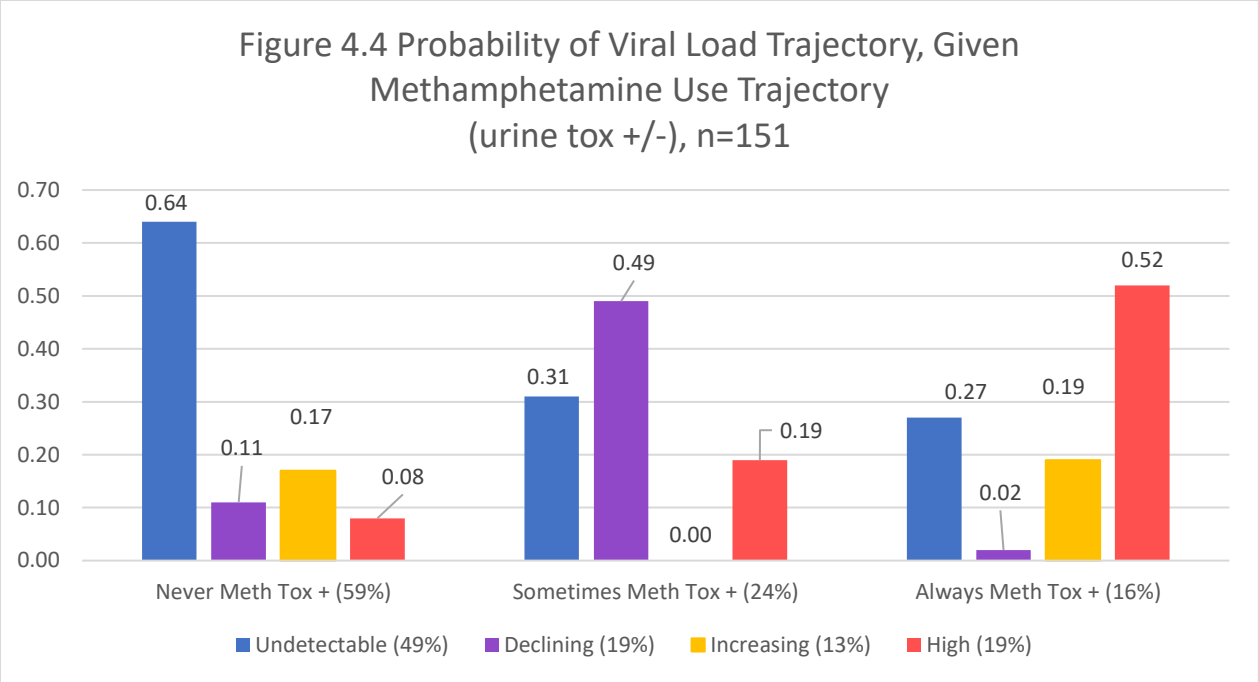
Figure 4.4 Probability of Viral Load Trajectory, Given Methamphetamine Use Trajectory (urine tox +/-), n=151
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
0.64
0.11
0.17
0.08
0.31
0.49
0.00
0.19
0.27
0.02
0.19
0.52
Never Meth Tox + (59%)
Sometimes Meth Tox + (24%)
Always Meth Tox + (16%)
Undetectable (49%)
Declining (19%)
Increasing (13%)
High (19%)

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Chapter 5. Concluding Remarks

It is an exciting time for biomedical HIV prevention. Between PrEP and TAsP, we have tools that can end the epidemic. Unfortunately, having the right tools is only part of the solution. Just as HIV risk is unevenly distributed among people in the United States, disproportionately affecting people of color, young people, and LGBTQ people, so too are barriers to biomedical HIV prevention dependent on social determinants of health. In practice, this means that the challenge is to design clinical and public health interventions and create policy with these disparities in mind to achieve health equity.

Through examining several stages of the HIV prevention continuum, this dissertation has several findings that can inform public health policy and future research. As demonstrated in Chapter 2 and 3, for PrEP to effectively prevent HIV infections among young people, support to increase uptake and facilitate persistence are needed. Current studies of long-acting PrEP are promising in this regard.[1] Increasing access to PrEP for people of color is also key. As discussed in Chapter 2, Black and Hispanic or Latino MSM and TGSM visiting a large community clinic had higher odds of self-identifying as good candidates for PrEP, but lower odds of initiating PrEP compared to White MSM and TGSM. For Black and Hispanic or Latino MSM and transgender women who did start PrEP, persistence did not differ from White patients (Chapter 3). This suggests that lowering barriers to PrEP initiation for people of color is a key priority to improve PrEP's effectiveness in community settings.

Chapter 3 also provided evidence that access to PrEP generally, in the form of low-cost or free insurance plans without a copay for PrEP medication, could improve persistence and ultimately reduce HIV incidence. If people had access to PrEP during times of highest risk, PrEP

could be more cost-effective in the long term than providing lifelong HIV treatment. Future studies examining use patterns of PrEP in the real world are critical to understanding this, as it is not yet known if people who use PrEP only during seasons of risks will assess their changing risk accurately enough to prevent HIV acquisition. Analyses of reasons for discontinuation are also key to developing prevention strategies that effectively address major barriers. Currently, a study is underway at the Los Angeles LGBT Center to survey patients who discontinued PrEP to determine the attributable fractions of changes in risk, insurance barriers, medication factors, and other reasons for missing doses or stopping PrEP.

Facilitating PrEP access for people who use methamphetamine and other sex drugs should be a priority to improve HIV prevention. As Chapter 2 demonstrated, MSM and TGSM who used sex drugs were not only more likely to have sexual risk factors for HIV, they were also more likely to self-identify as PrEP candidates and report PrEP use compared to those who reported no use of sex drugs. A recent study of PrEP persistence and stimulant use in San Francisco found that MSM who reported stimulant use did not have worse retention than MSM who reported no stimulant use, suggesting that fear of discontinuation should not deter providers from prescribing PrEP to people who use sex drugs.[2] On the other hand, a recently published analysis of simulant use in the iPrEX trial found that compared to participants with a negative urine drug screen, those who had positive urine drug screens for methamphetamine or other stimulants had five times higher odds of sub-optimal PrEP adherence as measured by dried blood spot.[3] With people who use stimulants, the priority for intervention may be supporting adherence. Coupled with findings from Chapter 4 that methamphetamine was associated with viremia among HIV positive MoCSM, this points to a need to prioritize primary biomedical

prevention for MSM who use methamphetamine. Incorporating support for adherence to primary prevention methods can ensure this strategy is maximally effective.

Using both behavioral and biomarker data provided rich insight to substance use careers. Because Chapter 4 found substantial heterogeneity in methamphetamine use patterns during an 18-month period, repeating this analysis over a longer time is warranted to examine how these trends change over periods of years. Understanding the implications of distinct substance use careers for HIV treatment outcomes can inform prevention strategies to address these comorbidities. Chapter 4 also contributes to more fully understanding of HIV disparities by demonstrating a link between methamphetamine use and viremia among MoCSM. Future studies incorporating data on adherence to antiretroviral treatment may more fully characterize this link.

In conclusion, addressing the HIV epidemic remains a complex public health challenge. The final contribution of this dissertation lies in the examining these questions in populations most affected by HIV in the United States, so that findings may be optimally relevant. By examining the relationship between methamphetamine use and viremia in a cohort of primarily Black and Latino MSM, we focused on groups most affected by HIV in the United States. By examining barriers and facilitators of PrEP use in a large LGBTQ-focused federally qualified health center, findings from these studies may prove useful to other clinics serving LGBTQ populations. Early data such as this from community settings is a crucial piece of the developing PrEP story. It adds real-world context to clinical trial findings, while working within the constraints likely common to PrEP providers (e.g., no dried blood spot measures of PrEP adherence in routine care, limited capacity to provide comprehensive PrEP retention support). Conducting public health research with and for populations most affected remains a key to promoting health equity.

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