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2021-08

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K. Coogan, S.A. Assoumou, MD MPH, S.M. Paniagua, MPH, P. Gonzalez, BS, J. Wang, MSc, C.G. Beckwith, MD, L. White, PhD, J.L. Taylor, MD, J.H. Samet, MD MA MPH, B.P. Linas, MD MPH. 2021. "HIV Pre-Exposure Prophylaxis and Buprenorphine at a Drug Detoxification Center during the Opioid Epidemic: Opportunities and Challenges" AIDS and Behavior, Volume 25, Issue 8, pp.2591-2598. https://doi.org/10.1007/s10461-021-03220-0

https://hdl.handle.net/2144/48423

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Author manuscript

AIDS Behav. Author manuscript; available in PMC 2022 August 01.

Published in final edited form as:

AIDS Behav. 2021 August ; 25(8): 2591–2598. doi:10.1007/s10461-021-03220-0.

HIV Pre-Exposure Prophylaxis and Buprenorphine at a Drug Detoxification Center during the Opioid Epidemic: Opportunities and Challenges

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Abstract

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Clinical trial registration: NCT02869776

Clinicaltrials.gov :

https://clinicaltrials.gov/ct2/show/NCT02869776?term=Sabrina+Assoumou&cond=HIV+HCV&rank=1

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Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) and buprenorphine decrease HIV acquisition. Between November, 2016 - July, 2017, we surveyed persons (N=200) at a drug detoxification center to assess their interest in PrEP and in buprenorphine, and to examine factors associated with such interests. Over the previous 6 months, 58% (117/200) injected drugs, 87% (173/200) used opioids, 50% (85/171) had condomless sex. Only 22% (26/117) of persons who injected drugs were aware of PrEP, yet 74% (86/116) and 72% (84/116) were interested in oral or injectable PrEP, respectively. Thirty-eight percent (47/125) of persons not receiving buprenorphine or methadone expressed interest in buprenorphine. After multivariable adjustment, Latinx ethnicity was associated with interest in PrEP (aOR: 3.80; 95% CI, 1.37–10.53), while male gender (aOR: 2.76; 95% CI, 1.21–6.34) was associated with interest in buprenorphine. Opportunities exist to implement PrEP and buprenorphine within drug detoxification centers.

Keywords

pre-exposure prophylaxis; persons who inject drugs; human immunodeficiency virus; medication for opioid use disorder; drug detoxification center

Introduction

Human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) and medications for opioid use disorder (MOUD) are evidence-based approaches to improve health outcomes in people who use drugs.[1,2] PrEP decreases HIV incidence among persons who inject drugs (PWID)[1] and is recommended by the Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force (USPSTF) for HIV prevention among PWID.[3,4] MOUD such as methadone and buprenorphine decrease morbidity and mortality among individuals with opioid use disorder.[5–7] In addition, buprenorphine is associated with decreased drug-related HIV risk.[8] As evidence-based tools, PrEP and MOUD should be integral to the ongoing efforts to decrease new HIV infections and overdose deaths among PWID during the opioid epidemic.[9,10]

Despite robust safety and efficacy data, PrEP and MOUD have not been widely adopted in real-world settings where individuals at high risk of substance use-related complications access care.[11–14] Drug detoxification centers serve individuals with active substance use disorders and represent important touchpoints for individuals who may lack access to or feel uncomfortable in traditional clinical settings.[15] Although drug detoxification centers are a potential venue to expand PrEP implementation for PWID and buprenorphine, little is known about the knowledge and interest in PrEP and buprenorphine among individuals accessing these facilities during the opioid epidemic.

Given the paucity of information on the feasibility and acceptability of PrEP among PWID, we undertook the current study to survey patients at a drug detoxification center to better understand their knowledge of and interest in HIV PrEP and outpatient medications for opioid use disorder.

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Methods

2.1 Participants and setting

We conducted a single site randomized trial comparing the real-world case notification of rapid testing to that of laboratory testing for HIV and HCV at a drug detoxification center. The study was conducted at the Boston Treatment Center (BOSTC) between November, 2016 and July, 2017.[16] The primary outcome was receipt of test results within two weeks. The survey for the current sub-analysis of the parent study was included as part of the initial questionnaire that we administered to all 200 patients included in the clinical trial.

BOSTC is the largest, short-term inpatient drug and alcohol detoxification center in the Boston metropolitan area, and its standard opioid withdrawal protocol during the study period was a 6day methadone or buprenorphine taper. BOSTC also had a case management program aimed at linking patients to substance use disorder treatment after discharge. The questionnaire focused on sex and drug use behaviors and overdose history. We also collected information on knowledge of and interest in HIV PrEP and buprenorphine. Eligibility criteria for the trial were as follows: 1) English-speaking; 2) 18 years or older; 3) Admission to BOSTC with a history of self-reported drug use; and 4) Willingness to provide locator information and sign a release of medical records form to enable collection of follow-up visit information from Boston Medical Center, a safety net hospital situated across from BOSTC. Persons reporting known HIV or HCV infection, and patients who had been tested for HIV and HCV within 6 months were excluded. Patients received a $20 gift card for completing the study. The study was approved by the Institutional Review Board of Boston University Medical Campus and a Certificate of Confidentiality was obtained from the National Institutes of Health.

2.2 Measures

A research assistant administered the questionnaire that collected information on knowledge and interest in PrEP and buprenorphine, including long-acting injectable forms of both. The questionnaire also collected demographics, substance use, psychiatric history (defined as having received a prescription for mental health disorder in the past 6 months), past HIV and HCV testing, sex and drug use behaviors, prior substance use treatment and overdose history. In terms of sexual history, we asked participants about the number and type of partners they had over the past 6 months as well as the frequency of condom use during the same time period. We also identified the proportion of patients with unstable housing, defined as living on the street or in an overnight shelter in the past 6 months.

Our primary outcomes of interest for this analysis was interest in PrEP and buprenorphine among BOSTC trial participants. We focused on buprenorphine because it is an MOUD that can be prescribed more easily in the outpatient setting with relatively lower barriers to linkage from drug detoxification centers when sufficient number of waivered prescribers exist in the locale. We also evaluated factors associated with patient interest in PrEP and buprenorphine. This study explores at-risk individuals' interest in the adoption of these evidence-based tools while seeking care at drug detoxification centers. Nonfatal overdoses are surrogates of substance use disorder severity and are predictive of future fatal

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overdoses.[17] As nonfatal overdoses represent potential windows of opportunity to engage patients in care, we present awareness and interest in PrEP in the subset of patients who had previously experienced a drug overdose.

2.3 Data Analysis

We used descriptive statistics to determine the proportion of individuals interested in PrEP and buprenorphine, separately. Variables significant in bivariate analysis and known potential confounders were included in logistic regression to determine factors associated with interest in PrEP and buprenorphine. We used 95% confidence intervals and all p-value significance levels were two-sided. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

A total of 341 individuals were screened for the parent randomized clinical trial and 200 participated, all of whom were included in this analysis. Patients who did not meet criteria for the randomized clinical trial were excluded for the following reasons: HIV or HCV testing within 6 months, 50% (71/141); refusal to take part in the study, 20% (28/141); unwilling or unable to share contact information, 17% (24/141); unable to sign a release form, 5% (7/141); HIV/HCV co-infection, 4% (5/141); non-English speaking, 3% (5/141); and age younger than 18 years <1% (1/141).

Among participants, mean [SD] age was 39 [10] years; 62% (124/76) were male; 45% (90/200) were White, 23% (46/200) Black, 23% (46/200) Latinx, 7% other (8/200) (Table 1). In addition, 10% (20/200) identified as gay or bisexual; 68% (136/200) had at least a high school level of education; and nearly 27% (55/100) had unstable housing.

3.1 HIV risk behavior, knowledge and interest in HIV preexposure prophylaxis including injectable formulation

The cohort reported multiple risk factors for HIV acquisition (Figure 1). Over the past 6 months, 58% (117/200) injected drugs and 31% (63/200) shared needles. Of individuals who reported being sexually active over the past 6 months (n=171), 50% (85/171) had condomless sex. In addition, of individuals who reported injecting drugs in the past 6 months (n=117), only 22% (26/117) were aware of PrEP and only 15% (18/117) knew that PrEP was recommended for people who inject drugs. When provided information about PrEP as an HIV prevention method (n=116), 74% (86/116) provided an answer and expressed interest in receiving a drug to prevent HIV, and 72% (84/116) specifically indicated an interest in an injectable form of HIV PrEP. We determined awareness and interest in PrEP in the subgroup of patients who had experienced a nonfatal drug overdose and found that similar to the larger cohort, 24% (24/98) had heard of PrEP and 73% (71/97) were interested in PrEP.

Given both sexual and injection risk behaviors in the cohort, we determined the factors associated with interest in PrEP in the full sample (n=200). In multivariable modeling, identifying as Latinx (OR: 3.80; 95% CI, 1.37–10.53) was independently associated with interest in PrEP after controlling for age, gender, race/ethnicity, risk behavior, unstable

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housing, HCV/HIV testing history, and prescription for mental health disorder. Eighty seven percent (40/46) of individuals identifying as Latinx were interested in PrEP compared to 80% (37/46) of Black/African American and 68% (62/90) of White participants (Figure 2).

3.2 Substance use history and interest in buprenorphine including long-acting injectable formulation

In terms of drug use history, heroin was the most common substance with 80% (159/200) reporting use in the past 12 months, followed by cocaine at 55% (110/200) and prescription opioids at 40% (80/200) (Table 1). Seventy nine percent (158/200) reported two or more substances. Forty nine percent (98/200) had a lifetime history of opioid overdose, and the same percentage had been prescribed naloxone for overdose prevention (Figure 3). Forty seven percent (94/200) reported ever using a drug to reverse an overdose. Over the past 6 months, 46% (92/200) had accessed substance use services in the form of drug detoxification programs, halfway house or residential facilities, day treatment programs for alcohol or drugs, and methadone treatment programs. Approximately one-half had received services at a drug detoxification center prior to the current admission. Of the participants who reported either heroin or prescription opioid use in the past 6 months (n=173), 26% (45/173) had been prescribed buprenorphine within the 6-month time frame (Figure 3). Of participants who had not been on prescribed buprenorphine or methadone in the past 6 months (n=125), 38% (47/125) were interested in being prescribed sublingual buprenorphine. Among individuals with either heroin or prescription opioid use (n=173), 47% (82/173) were interested in injectable buprenorphine. In multivariable modeling, male gender (OR: 2.76; 95% CI, 1.21–6.34) was independently associated with interest in buprenorphine after controlling for age, gender, race/ethnicity, unstable housing, injection drug use, past HIV/HCV testing, and prescription for mental health disorder.

Discussion

We investigated interest in both HIV pre-exposure prophylaxis (PrEP) and buprenorphine among individuals accessing acute drug detoxification services. In the midst of the opioid crisis, which has seen high rates of drug overdose, as well as several outbreaks of HIV infection among persons who inject drugs[10], interest has grown in developing models of care to deliver accessible substance use disorder treatment and HIV prevention services outside of traditional medical settings.[18,19] Experts have also called for reevaluating the role of drug detoxification centers, potentially restructuring these facilities into venues for initiating medication for opioid use disorder (MOUD) and addressing co-occurring conditions such as HIV.[20] Our work provides several key messages that can inform such efforts.

First, our findings underscore potential opportunities for implementing HIV PrEP in drug detoxification centers. The need for education and outreach is clear. We found that very little awareness of HIV PrEP existed among patients accessing drug detoxification centers, despite high self-reported risk for HIV acquisition through injection and sexual risk behaviors. Of note, high interest in PrEP was found once participants were informed of this biomedical prevention method. Also, participants expressed notable enthusiasm for the use of injectable forms of HIV PrEP. Interest in injectable PrEP is particularly timely

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given the recent release of HIV Prevention Trials Network (HPTN) 0083 findings, which demonstrated the effectiveness of injectable HIV PrEP in preventing HIV transmission.[21] This interest in PrEP was similar to prior studies showing that PWID are open to using PrEP once they learn about this effective intervention.[22] Although these data cannot speak to the proper model for PrEP implementation in drug detoxification centers, they suggest that interest in PrEP is present among PWID seen in these locations. Although information on the acceptability of long-acting injectable formulation of PrEP is limited, a qualitative study found that longer delivery methods would reduce barriers to daily oral PrEP adherence.[23] Our study adds to the current literature by suggesting a potential role for long-acting PrEP initiation at drug detoxification centers. These centers could be novel platforms for PrEP implementation in the midst of HIV outbreaks and in the context of the U.S. effort aimed at Ending the HIV Epidemic.[10,24] Future work should explore models for PrEP implementation in this setting.

Of interest, we found that participants who identified as Latinx were more likely to be interested in PrEP. Reasons for this finding are unclear. A recent study demonstrated gaps in knowledge about PrEP among Latinx men who have sex with men and Latinx transgender women, but this study did not delve into interest in PrEP.[25] There are however data showing that when compared to heterosexual White women, African American women were more likely to report potential use of PrEP.[26] The higher proportion of interest in PrEP among Latinx and Black/African-American patients is important as recent data show that these racial/ethnic groups are at higher risk for acquiring HIV, but are less likely to have access to PrEP. [27,28] Our findings support additional studies to increase uptake among these groups.

Second, the current study highlights important areas of future research that will be foundational to any successful effort to utilize drug detoxification centers as venues for initiating buprenorphine, including the need for qualitative research exploring reasons why many patients might not be interested in this medication. It is essential to understand why some patients who access drug detoxification centers are not interested in starting buprenorphine treatment. Potential reasons might include a preference to treat opioid withdrawal with methadone given that this medication is a full opioid agonist (i.e. it can be initiated soon after heroin use without precipitating opioid withdrawal) and competing priorities such as housing, barriers to outpatient care including transportation, or a lack of readiness to change substance use. Our survey did not probe deeper to understand the motivators and barriers to initiating buprenorphine in detoxification facilities. What is clear, however, is that simply offering buprenorphine to patients entering detoxification centers might not result in a majority of patients initiating and continuing this medication. Nevertheless, the fact that nearly 4 in 10 patients not on MOUD in the past 6 months were interested in initiating buprenorphine suggests an important opportunity in drug detoxification centers. Buprenorphine initiation coupled with direct linkage to low-barrier bridge clinic programs or Office-Based Addiction treatment (OBAT) programs [29] has the potential to enhance the care continuum for individuals with OUD and reduce loss to follow-up between acute treatment and outpatient care settings.

Third, future research investigating interest in MOUD in drug detoxification centers should explore the potential to deliver injectable long-acting formulations of buprenorphine in this

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setting. A monthly injectable form of buprenorphine was FDA-approved for the treatment of opioid use disorder in November, 2017 but was not routinely available clinically at nearby institutions until late 2018, after the study period. Long-acting formulations have the potential to improve retention on medications, but the real-world effectiveness of these MOUD formulations when initiated in acute treatment settings is still unknown. Injectable buprenorphine has the potential to address structural barriers to sublingual buprenorphine adherence faced by some patients with unstable housing, including medication loss, theft, pressure to sell or trade medication, and ability to obtain regular refills.[30] The real-world effectiveness of monthly injectable buprenorphine initiated in detoxification settings merits future study. Simply initiating long-acting medications may not lead to retention on MOUD without additional support. For example, a prior study demonstrated that approximately half of patients on injectable extended-release naltrexone discontinued this medication after the first injection.[31] Buprenorphine and extended-release naltrexone have different mechanisms of action, and it is not known how retention on long-acting buprenorphine will compare to extended-release naltrexone. Patients initiating long-acting injectable buprenorphine may require case management to ensure linkage to a long-term care setting equipped to continue this buprenorphine formulation. Ongoing studies might provide some additional information on the best approach to integrate injectable formulations within existing care models with the goal of improving retention on MOUD and patient outcomes.[32]

Our findings confirm that the potential for drug detoxification centers to reach patients not previously treated with buprenorphine for opioid use disorder is high. Consistent with prior work, just one-third of participants with a history of heroin or prescription opioid use had been prescribed buprenorphine in the past 6 months.[12] Approximately 40% of individuals who had not been prescribed buprenorphine and were not on methadone reported interest in buprenorphine initiation, and a similar proportion were open to an injectable buprenorphine formulation. Results suggest substantial opportunity to increase buprenorphine initiation in drug detoxification facilities; they also highlight the challenges of meeting the needs of all patients with opioid use disorder with a single MOUD approach, as a little over one-half of participants were not interested in buprenorphine.

Limitations to the current study include the cross-sectional study design and the use of a single, urban site located in close proximity to significant MOUD infrastructure. Although these factors might influence generalizability to rural or lower-resource urban settings, we provide novel information on the opportunity to expand PrEP and buprenorphine initiation, including the potential role for long-acting injectable formulations, in non-traditional settings such as acute detoxification centers. In addition, we did not ask participants about fentanyl use as it was much less prevalent in our location at the time of the study; however, we obtained some detailed information about other substances used including heroin, amphetamines, crack/cocaine and noted the use of multiple substances.

Conclusion

We documented limited awareness of HIV PrEP among people entering a substance use treatment center, but observed enthusiasm for this biomedical prevention method once patients were made aware. We also identified an opportunity to expand MOUD initiation

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with buprenorphine during a stay at substance use treatment centers. Recent and pioneering studies have shown that starting MOUD is feasible and acceptable in various settings such as jails or prisons, HIV and HCV specialty clinics, and inpatient settings during reachable moments.[33–36] The current study provides additional data on potentially initiation these treatments in substance use treatment centers.

The potential for drug detoxification centers to become venues for addressing the syndemics of opioid use disorder and HIV is real, and the current findings frame some of the significant challenges and opportunities inherent in this approach. Future studies should further explore how to increase interest in buprenorphine among drug detoxification patients during the opioid overdose epidemic and evaluate implementation strategies for PrEP and MOUD and in these facilities.

Acknowledgement:

The authors would like to thank study participants and our research team for their contributions to this work.

Funding:

This work was supported by the National Institute of Allergy and Infectious Diseases [P30AI042853 Providence/Boston Center for AIDS Research collaborative developmental grant to S.A.A]; and the National Institute of Drug Abuse [R25DA035163 pilot award to S.A.A, K23DA044085 to S.A.A, R01DA046527 to B.P.L, and P30DA040500 to B.P.L]. The content is solely the responsibility of the authors and does not necessarily represent the official views of National Institutes of Health.

Findings were presented as a poster at the College on Problems of Drug Dependence (CPDD), San Diego, California, June 11th, 2018.

Abbreviations:

MA	Massachusetts
RI	Rhode Island
USA	United States of America

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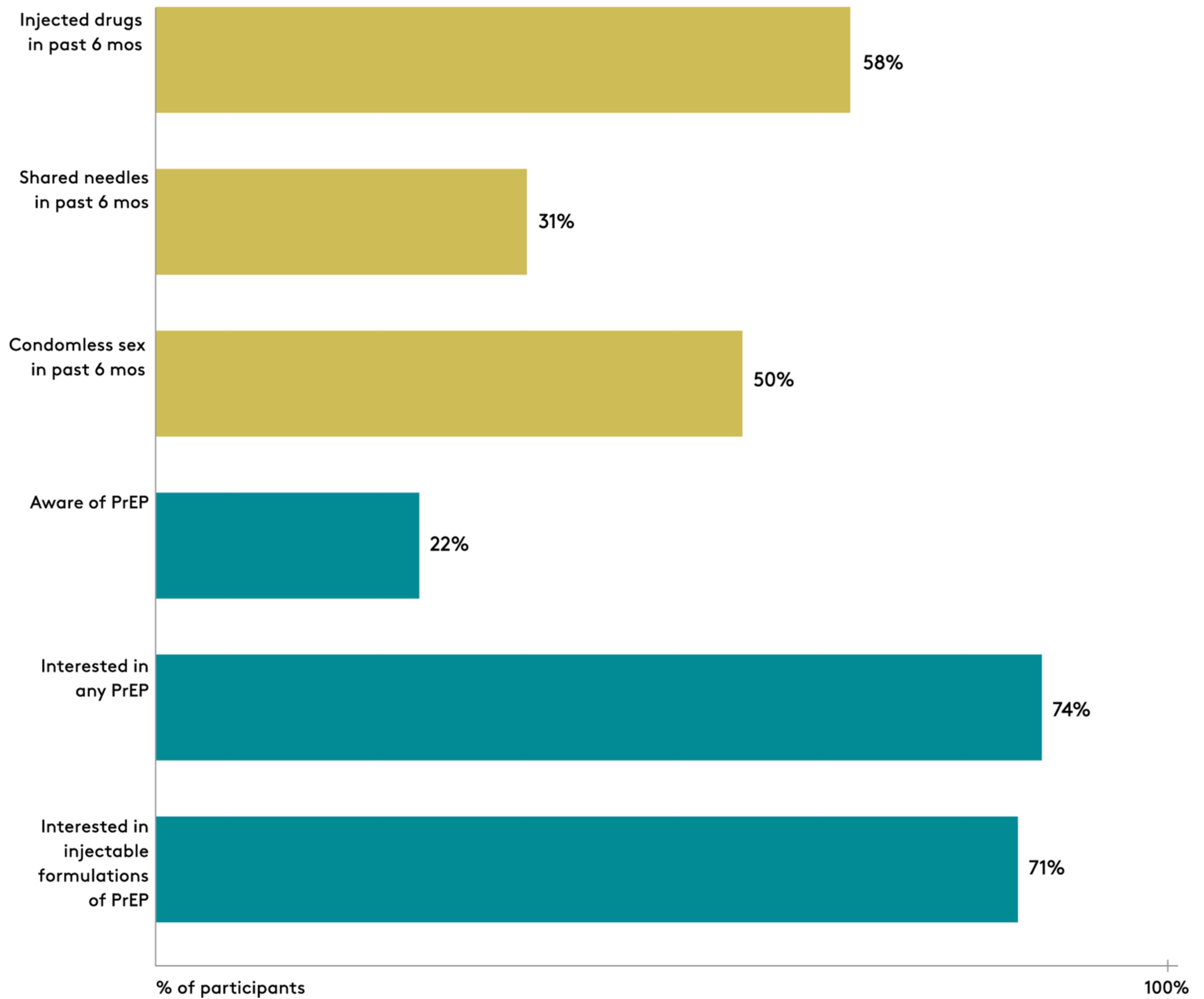

Figure 1:

Human immunodeficiency virus (HIV) risk and interest in pre-exposure prophylaxis (PrEP) among participants recruited at a drug detoxification center.

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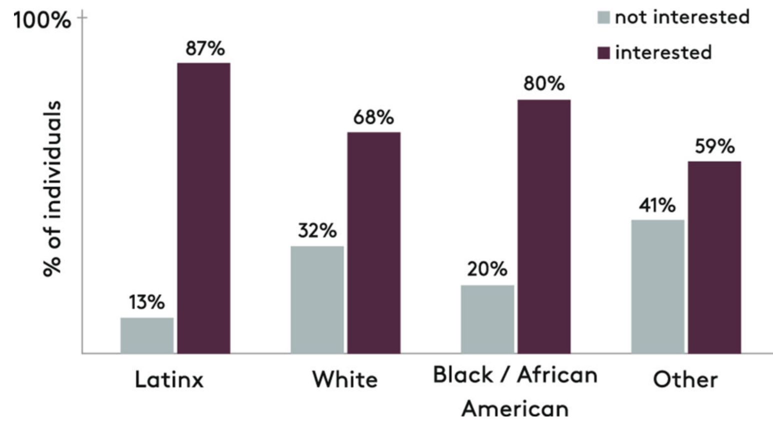

Figure 2:
Interest in human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) stratified by race/ethnicity of participants recruited at a drug detoxification center.

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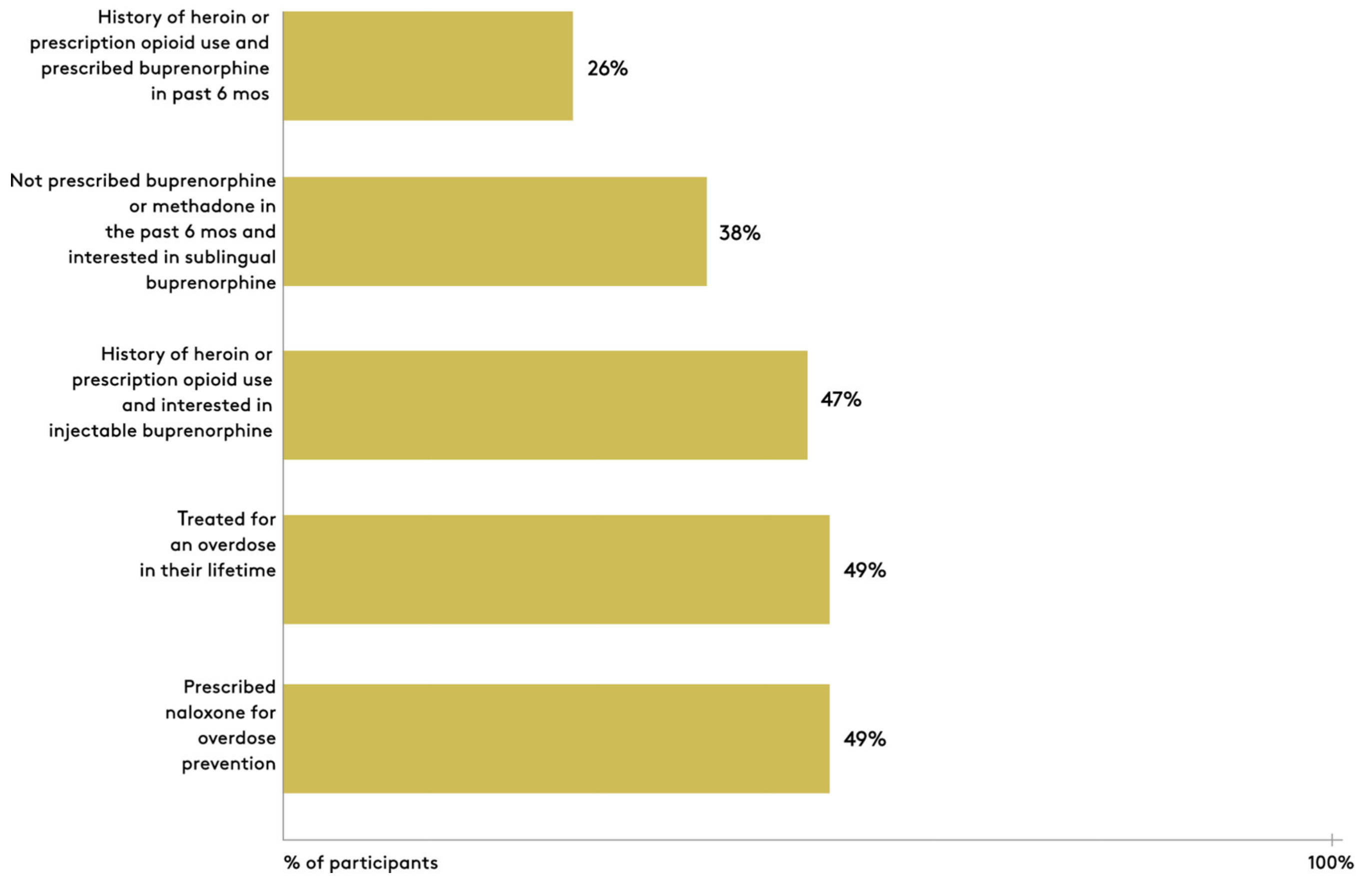

Figure 3:
Experience and interest in buprenorphine, and history of nonfatal drug overdose among participants recruited at a drug detoxification center.

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Table 1.

Baseline characteristics of participants seen at a drug detoxification center (*N*=200)

Characteristic		(N=200)
Mean age (SD) --- years		39 ± 10
Gender ---no. (%)	Female	76 (38)
	Male	124 (62)
Race/Ethnicity ---no. (%)	Latinx	47 (23)
	White	90 (45)
	Black	46 (23)
	Other	17 (8)
Education level ---no. (%)	< High School	9 (5)
	High School	136 (68)
	> High School	55 (27)
Unstable Housing* ---no. (%)		55 (27)
Sexual Orientation ---no. (%)	Straight	180 (90)
	Gay	7 (4)
	Bisexual	13 (6)
Substance use ---no. (%)	Heroin	159 (80)
	Sedative	59 (30)
	Tranquilizers	91 (46)
	Amphetamines	57 (29)
	Prescription opioids	80 (40%)
	Inhalants	8 (4%)
	Cocaine/crack	110 (55%)
	Hallucinogens	8 (4%)
	Two or more substances	158 (79%)
Substance use services in past 6 mo. —no. (%)		92 (46%)
Prescription for mental health disorder in past 6 mo.---no. (%)		70 (35%)

*Defined as living on the street or in an overnight shelter in the past 6 months.