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Post-exposure prophylaxis use and recurrent exposure to HIV among men who have sex with men who use crystal methamphetamine

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Abstract

Background—Men who have sex with men (MSM) who use crystal methamphetamine (CM) are at increased risk for HIV infection. Post-exposure prophylaxis (PEP) is a useful HIV prevention strategy if individuals are able to identify high-risk exposures and seek timely care, however to date there has been limited data on the use of PEP by CM users.

Methods—A retrospective cohort study of all PEP prescriptions (N=1,130 prescriptions among 788 MSM) at Fenway Community Health in Boston, MA was undertaken. Multivariable models were used to assess the association between CM use during exposure (7.4% used CM during exposure) and chronically (7.4% of MSM were chronic CM users) and individual-level and event-level outcomes among MSM who used PEP at least once.

Results—Compared to those who had not used CM, MSM PEP users who used CM more frequently returned for repeat PEP (aOR 5.13, 95%CI 2.82 to 9.34) and were significantly more likely to seroconvert over the follow-up period (aHR 3.61, 95%CI 1.51 to 8.60). MSM who used CM had increased odds of unprotected anal intercourse as the source of exposure (aOR 2.12, 95%CI 1.16 to 3.87) and knowing that their partner was HIV infected (aOR 2.27, 95%CI 1.42 to 3.64).

Conclusions—While MSM who use CM may have challenges accessing ART in general, these data highlight the fact that those who were able to access PEP subsequently remained at increased risk of HIV seroconversion Counseling and/or substance use interventions during the PEP course should be considered for CM-using MSM.

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Keywords

post-exposure prophylaxis; HIV prevention; crystal methamphetamine; men who have sex with men

1. INTRODUCTION

Crystal methamphetamine is a highly addictive psychostimulant that has been linked to high-risk sexual behavior and incident HIV infection among men who have sex with men (MSM).(Gonzales et al., 2010; Koblin et al., 2006; Mayer et al., 2013) The use of crystal methamphetamine is considerably more prevalent among MSM in the United States than in the general population, with the prevalence of use nearly 10 times greater.(Colfax and Shoptaw, 2005; Mimiaga et al., 2012b) It has been well established that crystal methamphetamine use is predictive of higher risk sexual encounters, including low rates of condom use, an increase in number of sexual partners, including anonymous partners, and prolonged sexual encounters spanning multiple days.(Benotsch et al., 2012; Halkitis et al., 2001; Rajasingham et al., 2012)

Post-exposure prophylaxis (PEP) consists of a 28-day course of antiretroviral therapy (ART) given prophylactically within 72 hours of a high-risk exposure.(Smith et al., 2005) Although PEP efficacy in humans has never been tested in a randomized controlled trial, it has been shown to reduce the odds of HIV seroconversion in animal models(Tsai et al., 1995) and following health care workers' needle stick exposures in a nested case control study.(Cardo et al., 1997; Jain and Mayer, 2014) Although crystal methamphetamine-using MSM might benefit from biomedical HIV prevention strategies such as PEP or pre-exposure prophylaxis (PrEP), concerns related to the ability of users to adhere to ART regimens have limited prescription of PEP for this subpopulation.(Landovitz et al., 2012; O'Connor, 1999; Oldenburg et al., 2013) Furthermore, evidence suggests that MSM who use stimulants are significantly less likely to be aware of PEP as an HIV prevention strategy, which further limits its use among this group.(Liu et al., 2008) A key component to the success of PEP is an individual's ability to identify high-risk exposures, know where to get treatment, and seek medical attention within 72 hours, in addition to their ability to complete the prescribed regimen.

The purpose of the present study is two-fold. Firstly, we sought to characterize the effect of event-level and chronic crystal methamphetamine use and sexual risk behavior during the exposure that led to PEP, compared to individuals who accessed PEP but had not used crystal methamphetamine. Event-level crystal methamphetamine use may affect risk-taking behavior differentially compared to chronic use, and thus we attempt to understand the effect of crystal methamphetamine use at the time of event independently of whether or not the individual is a chronic methamphetamine user. Secondly, we sought to assess the relationship between repeat PEP use and long-term outcomes following presentation for PEP in MSM with crystal methamphetamine use compared to those who had not used crystal methamphetamine. A better understanding of the context of risk prior to, and after, first PEP use and the trajectory of subsequent PEP use among MSM who use crystal

methamphetamine will help to inform the optimal deployment of biomedical HIV prevention strategies for this group of MSM.

2. METHODS

2.1. Study Sample

Data for this study were derived from a retrospective longitudinal review of all PEP users at Fenway Community Health in Boston, MA between July 1, 1997 and August 1, 2013. Full methods for the study have been previously reported.(Jain et al., n.d.) Briefly, patients with a prescription for a one month course of an antiretroviral medication combination in their electronic medical record during this time period who were HIV-uninfected were screened for study eligibility. Inclusion criteria included: 1) age 18 years or older at time of first PEP visit; 2) documentation of sexual and/or non-occupational intravenous drug needle exposure to HIV; and 3) HIV negative antibody or RNA test at time of baseline PEP visit. Patients with confirmatory positive HIV serostatus within 30 days of initiating PEP, or who received a prescription for PEP but did not follow up in person, or those who prescribed PEP for occupational or non-sexual or intravenous needle exposure, or enrolled in a PEP clinical trial, were excluded from this analysis. The present analysis was limited only to participants who reported a male, non-transgender, gender identity who reported having male partners. The Institutional Review Board at Fenway Community Health approved all study procedures.

2.2. Measures

All data were extracted from patients' electronic medical records.

2.2.1. Crystal methamphetamine use—Patients were determined to have crystal methamphetamine dependence if it was documented in their medical record that they had been referred for treatment for methamphetamine use. Patients were asked by providers if they had used any substances at the time of the exposure that led to seeking PEP, and crystal methamphetamine use was documented for patients reporting that substance.

2.2.2. Event-level HIV risk—Patients who presented for PEP were routinely asked by the treating clinician about risk behaviors during the incident that led to seeking PEP, including substance use, if the exposure was via sexual or intravenous needle exposure, and, for sexual exposures, if it was consensual or forcible, and if the patient was the receptive or insertive partner. Patients were also asked if a condom was used, and if so, if it broke or was removed by the patient or partner, as well as the HIV status (know positive or unknown) and treatment status of partner (on treatment, not on treatment, or unknown treatment status).

2.2.3. PEP regimen—Prescribed antiretroviral regimen, regimen completion, reasons for non-completion or modifying regimen, adverse effects, and follow up at 1, 3, and 6 months after PEP prescription were extracted from the electronic health records, and recorded. Patients were coded as having completed their PEP regimen if it was documented in their medical record that they had completed the entire regimen without missing doses. Repeat PEP prescriptions were recorded for patients who returned for additional PEP prescriptions.

2.2.4. HIV testing—Any positive HIV antibody or plasma RNA test, including a rapid whole blood finger stick assay or serum antibody and/or plasma viral load, was required for diagnosis of an incident HIV infection.

2.2.5. Demographics—Patients were classified as MSM if they reported male gender identity when they presented for PEP, and reported having exclusively male or both male and female partners. Other demographic information extracted included age at first PEP visit, whether or not patients were enrolled in primary care at the community health clinic, race/ethnicity (coded as White/Caucasian, Latino/Hispanic, Black/African American, Asian/Pacific Islander, and Other), any history of homelessness or unstable housing, any history of sex work, and insurance status (coded as any insurance versus no insurance).

2.2.6. Mental Health Diagnoses—Patients were coded as having a diagnosis of depression, anxiety, bipolar (I or II), and/or attention deficit disorder if it was documented in their medical record that they had received treatment (psychotherapy and/or pharmacotherapy) for the disorder.

2.3. Statistical Methods

All analyses were restricted to MSM. Proportions for categorical variables and means and standard deviations for continuous variables were calculated for patients who had a documented crystal methamphetamine use disorder and those who did not. The bivariate association between having a crystal methamphetamine use disorder and repeat PEP use was assessed using logistic regression models. A Cox proportional hazards model was used to assess the association between having a crystal methamphetamine use disorder and HIV seroconversion during the study follow-up period (post initial PEP course). Multivariable models were fitted for both outcomes adjusting for age at first PEP visit, insurance status (categorized as any or none), primary care status, history of homelessness or sex work, race/ethnicity, year of first PEP visit, and treatment for depression, anxiety, attention deficit disorder, and/or bipolar (I/II) prior to first PEP visit. Due to variability of follow-up following PEP visits, as a sensitivity analysis a separate multivariable Cox proportional hazards model was built restricting only to patients who were engaged in primary care at the clinic.

The association between PEP events, including unprotected anal intercourse (UAI) as the reason for seeking PEP, unprotected receptive anal intercourse (URAI) as the reason for seeking PEP among unprotected consensual exposures, knowing the partner was HIV-infected, and receiving a 3-drug regimen (versus 2-drug), and 1) crystal methamphetamine use during the exposure and 2) having a documented crystal methamphetamine use disorder were modeled using logistic generalized estimating equation (GEE) models, to account for the clustering induced by multiple PEP visits in a single individual. Models for the effect of crystal methamphetamine use at the time of exposure were adjusted for having a documented crystal methamphetamine use disorder to control for potential confounding by crystal methamphetamine use disorders. However, models for the effect of crystal methamphetamine use disorders on each of the 4 outcomes did not include crystal methamphetamine use at the time of exposure as a covariate due to concerns related to

conditioning on an intermediate, which could induce bias in the presence of unmeasured confounding of the effect of crystal methamphetamine use during exposure and the outcome. Multivariable models for each outcome were built using logistic GEE models that adjusted for additional potential sources of confounding, including age at PEP visit, year of PEP visit, primary care status, insurance status (any or none), race/ethnicity, and diagnosis of and treatment for depression, anxiety, attention deficit, and/or bipolar (I/II) disorder prior to first PEP visit.

3. RESULTS

3.1. Descriptive statistics

Of 788 MSM who sought PEP between July 1, 1997 and August 1, 2013, 58 (7.4%) had a documented chronic crystal methamphetamine use disorder at the time of their first PEP prescription. Among the 788 MSM who sought PEP, there were 1,130 PEP prescriptions during the observation period (range 1 to 15 prescriptions per patient). Of these, crystal methamphetamine was used during 84 (7.4%) of exposures that led to seeking PEP. Median follow-up time was 1.9 years (IQR 1.1 to 4.6 years) among MSM with a crystal methamphetamine use disorder and 1.0 (IQR 0.1 to 3.1 years) among MSM without a crystal methamphetamine use disorder. Among individuals who were engaged in primary care at the health center, median follow-up time was 2.1 years among individuals with a crystal methamphetamine use disorder (IQR 1.3 to 4.6 years) and 2.2 years (IQR 0.8 to 4.6) among individuals without one. Table 1 presents descriptive characteristics of the sample with and without a crystal methamphetamine use disorder. Crystal methamphetamine users were more frequently engaged in primary care at the site where they presented for PEP. They also more frequently were white/Caucasian, had a history of homelessness or unstable housing and sex work, and had documented psychiatric disorders at the time of first PEP, including major depressive disorder, anxiety disorder, and attention deficit disorder.

Table 2 lists characteristics of each PEP visit, by event-level crystal methamphetamine use as well as by whether or not individuals had crystal methamphetamine use disorders. Individuals who used crystal methamphetamine at the time of exposure as well as those with chronic use disorder more frequently reported UAI as the source of exposure, whereas those without any crystal methamphetamine use more frequently endorsed condom failure as the event that led to exposure than crystal methamphetamine users. Individuals who had used crystal methamphetamine (both at the time of exposure and chronically) more frequently knew that their partner was HIV infected, but did not know their treatment status. Use of other sex-enhancing drugs was limited. No patients reported the recreational use of erectile dysfunction medication. The use of amyl nitrites (poppers) was reported for 12 exposures (1.1% of all exposures), of which 2 (2.4%) were concurrent with crystal methamphetamine use.

3.2. Individual-level analyses

Table 3 lists factors related to long-term outcomes after PEP prescription(s). Individuals with a documented crystal methamphetamine use disorder had significantly increased incidence rate of HIV infection over the follow-up period (aHR 3.61, 95% CI 1.51 to 8.60),

and had greater odds of repeat PEP use (aOR 5.13, 95% CI 2.82 to 9.34) compared to non-users during the follow-up period. As a sensitivity analysis, we restricted the entire sample only to individuals engaged in primary care at Fenway Health. There was no difference between sensitivity analyses and primary analyses in the effect of crystal methamphetamine use disorder on HIV incidence (aHR 3.39, 95% CI 1.42 to 8.07) or odds of repeat PEP (aOR 5.12, 95% CI 2.72 to 9.65) in the subset of patients who were primary care patients at Fenway Health.

3.3. Event-level analyses

Table 4 shows the association between both crystal methamphetamine use at the time of exposure as well as having a documented crystal methamphetamine use disorder and PEP visit-level characteristics. Crystal methamphetamine use at the time of exposure was associated with increased odds of UAI as the route of exposure leading to seeking PEP (aOR 3.01, 95% CI 1.36 to 6.71), being the receptive partner among unprotected consensual exposures (aOR 2.98, 95% CI 1.55 to 5.75), and receiving a three-drug regimen compared to a two-drug regimen (aOR 1.99, 95% CI 1.16 to 3.40), independent of having an underlying crystal methamphetamine use disorder. Patients with a crystal methamphetamine use disorder had significantly greater odds of UAI as the route of exposure that led them to seek PEP (aOR 2.12, 95% CI 1.16 to 3.87), being the receptive partner among unprotected consensual exposures (aOR 1.98, 95% CI 1.04 to 3.78), having a known HIV-infected partner (aOR 2.27, 95% CI 1.42 to 3.64), and receiving a three-drug regimen (aOR 3.19, 95% CI 1.88 to 5.40).

4. DISCUSSION

The results of this study indicate that a substantial proportion of Boston MSM who sought PEP following a high-risk exposure had used crystal methamphetamine, and that these individuals knew where and how to seek treatment within 72 hours of the exposure. MSM who used crystal methamphetamine were more likely to return for repeat PEP than those who did not use this stimulant, suggesting high levels of recurrent risk, as well as the ability to identify risky exposures and access care quickly following exposure. However, despite repeat PEP use, crystal methamphetamine-using MSM were more likely to become infected with HIV compared to MSM who did not report use of the drug.

Crystal methamphetamine use at the time of exposure was associated with UAI as the source of potential exposure (as compared to either condom failure or oral intercourse), which is in line with previous evidence that event-level crystal methamphetamine use is associated with risk-taking behavior.(Benotsch et al., 2012; Buchacz et al., 2005; Mimiaga et al., 2012b) In addition to event-level crystal methamphetamine use, individuals who had a chronic crystal methamphetamine use disorder more frequently reported UAI as the potential exposure that led to seeking PEP. Crystal methamphetamine-using MSM were also more frequently prescribed 3-drug regimens, likely due to the providers' perception of especially high-risk exposures. Although individuals with a crystal methamphetamine use disorder more frequently reported knowing their partner at the time of exposure was HIV infected, event-level methamphetamine use was not associated with knowing the partner's HIV status. It is

possible that, given the increased HIV risk in this population, within sexual networks for crystal methamphetamine-using MSM, individuals are more likely to know their partners are HIV infected. The inclusion of both event-level and chronic crystal methamphetamine use allows for a more nuanced understanding of the effect of crystal methamphetamine use on event-level risk behavior. Given that not all chronic methamphetamine users used crystal methamphetamine at each exposure, and not all individuals who used crystal methamphetamine had been referred to treatment for crystal methamphetamine use, these results demonstrate the importance of assessing both event-level use as well as chronic use.

The results of this study provide important evidence that MSM who use crystal methamphetamine who are engaged in culturally-competent care are able to obtain PEP, but their recurrent risk behavior and increased rates of HIV incidence suggest that the biobehavioral prevention interventions offered during an PEP course may not sufficiently attenuate the increased risk. Pre-exposure prophylaxis (PrEP)(Grant et al., 2010), consisting of a once-daily pill taken prior to potential HIV exposures, may be a convenient and important method of sustained prevention for many of these individuals, although further studies are needed to examine the transition from PEP to PrEP in this population. The PEP visit might also provide an educable moment, where individuals increase their engagement in self-care, and obtain experience taking daily medication for chemoprophylaxis. Furthermore, concurrently addressing substance use and providing appropriate treatment is essential for effective HIV prevention, although the literature for effective interventions for crystal methamphetamine use is mixed. Cognitive behavioral therapy (CBT) and contingency management (CM) are two approaches that have been shown to be efficacious at achieving abstinence from stimulant use but with limited long-term effects.(Rawson et al., 2006) Recent work has focused on the integration of behavioral activation (BA) with CM, which has shown promise in sustaining the effects of CM alone over time.(Mimiaga et al., 2012a) Future PEP and/or PrEP interventions could include a BA/CM component in addition to provision of PEP or PrEP. To date, most HIV prevention interventions among substance users have shown modest effects(Meader et al., 2013) , and most HIV prevention interventions for drug users have focused on injection drug users.(Shoptaw et al., 2013) Community-based substance use treatment programs have also been implemented with this population(Carrico et al., 2014; Shoptaw et al., 2008), which may provide an opportunity for identification of individuals who could benefit from longer-term HIV prevention strategies such as PrEP while simultaneously addressing substance use. A combined substance use and HIV prevention approach may be especially effective in reducing HIV transmission and acquisition.

The results of this study must be considered in the context of several limitations. As previously mentioned, this study was retrospective, and follow-up time varied widely. We attempted to control for potential biases through a variety of sensitivity analyses, however there could still be residual biases inherent in these data. Overall, individuals who had a crystal methamphetamine use disorder had longer follow-up time than those without, but there was no difference in median follow-up time when restricting only to individuals engaged in primary care. Sensitivity analyses restricting only to those engaged in primary care did not differ from primary analyses. It is possible that some individuals may have had a crystal methamphetamine use disorder that had not been diagnosed or treated and as such

was not in the patient's medical record, which could lead to misclassification. Similarly, there could have been misclassification if individuals did not want to disclose substance use during exposure to providers. We did not have data on the HIV viral load of patients' HIV-infected partners, which would have provided additional insight into HIV risk. In addition, due to low rates of documentation of regimen completion, we were unable to assess differences in PEP regimen completion between crystal methamphetamine users and non-users. Future work should carefully consider completion of PEP among MSM who use crystal methamphetamine. Finally, these data represent a single clinic in Boston, and results may not be generalizable to other sites. However, despite these limitations, these data present one of the largest cohorts of individuals on PEP with a long period of follow-up, including one of the largest cohorts of crystal methamphetamine-using MSM who have initiated PEP. As such, we believe that these data provide useful and valuable evidence regarding the utility of PEP for HIV prevention among MSM who use crystal methamphetamine, and suggest that many of these MSM could potentially benefit from PrEP.

In summary, the results of this study showed that many MSM who use crystal methamphetamine were able to identify high-risk exposures and seek PEP in the context of culturally competent clinical care. Crystal methamphetamine use was associated with particularly high-risk exposures, and despite seeking out PEP and being engaged in care, these individuals remained at recurrent high risk of HIV, as evidenced by higher rates of HIV seroconversion as well as repeat PEP use. Despite accessing PEP, these individuals remained at heightened risk of HIV seroconversion. Therefore, the incorporation of more intensive counseling during the PEP course and/or implementation of structured, evidence-based biobehavioral interventions upon completion of PEP should be strongly considered for crystal methamphetamine using MSM to curb HIV acquisition in this high-risk population.

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Table 1

Descriptive baseline characteristics among MSM with a documented crystal meth abuse disorder (N=58) and without a crystal meth use disorder (N=730)

	Documented Crystal Meth Use Disorder	No Crystal Meth Use Disorder	Overall	*P*-value
Age at first NPEP visit, mean (SD)	32.9 (9.8)	34.6 (9.5)	34.5 (9.5)	0.18
Engaged in primary care at the clinic	53 (91.4%)	461 (63.2%)	514 (65.2%)	<0.001
Race/ethnicity				
White/Caucasian	52 (89.7%)	533 (73.0%)	585 (74.2%)	0.06
Latino/Hispanic	1 (1.7%)	84 (11.5%)	85 (10.8%)	
Black/African American	2 (3.5%)	42 (5.8%)	44 (5.6%)	
Asian/Pacific Islander	1 (1.7%)	34 (4.7%)	35 (4.4%)	
Other	2 (3.5%)	37 (5.1%)	39 (5.0%)	
History of homelessness or unstable housing	6 (10.3%)	9 (1.2%)	15 (1.9%)	<0.001
History of sex work	4 (6.9%)	8 (1.1%)	12 (1.5%)	
Any insurance	36 (62.1%)	473 (64.8%)	509 (64.6%)	0.008
Depression prior to first PEP visit	29 (50.0%)	166 (22.7%)	195 (24.8%)	<0.001
Anxiety disorder prior to first PEP visit	22 (37.9%)	153 (21.0%)	175 (22.2%)	0.005
Attention deficit disorder prior to first PEP visit	9 (15.5%)	56 (7.7%)	65 (8.3%)	0.046
Bipolar I/II disorder prior to first PEP visit	6 (10.3%)	19 (2.6%)	25 (3.2%)	0.007
HIV seroconversion	9 (15.5%)	30 (4.1%)	39 (5.0%)	0.001
Repeat PEP	33 (56.9%)	134 (18.4%)	167 (21.2%)	<0.001

Table 2

Characteristics of PEP exposures and regimens by event-level crystal methamphetamine use (N=84) compared to no crystal methamphetamine use (N=1,046) and by chronic crystal methamphetamine use compared to no chronic methamphetamine use

	Crystal Meth Use at Time of Exposure	No Crystal Meth Use	*P*-value	Documented Crystal Meth Use Disorder[1]	No Crystal Meth Use Disorder	*P*-value	Overall
Reason for NPEP access							
Unprotected anal sex	68 (81.0%)	569 (54.4%)	<0.001	110 (74.3%)	527 (53.7%)	<0.001	637 (56.4%)
Unprotected oral sex	3 (3.6%)	74 (7.1%)	0.27	3 (2.0%)	74 (7.5%)	0.008	77 (6.8%)
Condom failure	7 (8.3%)	344 (32.9%)	<0.001	25 (16.9%)	326 (33.2%)	<0.001	351 (31.1%)
Rape	3 (3.6%)	31 (3.0%)	0.74	5 (3.4%)	29 (3.0%)	0.80	34 (3.0%)
Needle Sharing	5 (6.0%)	2 (0.2%)	<0.001	4 (2.7%)	3 (0.3%)	0.007	7 (0.6%)
HIV status of partner							
Known infected – on treatment	8 (9.5%)	143 (13.7%)		20 (13.5%)	131 (13.3%)		151 (13.4%)
Known infected – not on treatment	2 (2.4%)	44 (4.2%)	<0.001	1 (0.7%)	45 (4.6%)	<0.001	46 (4.1%)
Known infected – unknown treatment	32 (38.1%)	173 (16.5%)		51 (34.5%)	154 (15.7%)		205 (18.1%)
Unknown status	42 (50.0%)	686 (65.6%)		76 (51.4%)	652 (66.4%)		728 (64.4%)
Tenofovir-based treatment regimen	70 (84.3%)	796 (77.3%)	0.17	120 (82.8%)	746 (77.1%)	0.13	866 (77.8%)
Three-drug regimen	59 (70.2%)	476 (45.5%)	<0.001	97 (65.5%)	438 (44.6%)	<0.001	535 (47.4%)

[1] Individuals could have had more than one NPEP visits; numbers do not add up to 58 (total number of individuals with a documented crystal methamphetamine use disorder)

Table 3

Association between having documented crystal methamphetamine dependence and 1) HIV seroconversion and 2) returning for >1 PEP course

	HIV seroconversion[1]		Repeat NPEP Use[2]	
	HR (95% CI)	**aHR (95% CI)**	**OR (95% CI)**	**aOR (95% CI)**
CM dependence	***2.49 (1.18 to 5.26)***	***4.04 (1.71 to 9.53)***	***5.87 (3.38 to 10.2)***	***5.30 (2.87 to 9.79)***
Age at first PEP visit		*0.95 (0.91 to 0.99)*		1.01 (0.99 to 1.03)
In primary care at Fenway Health		4.00 (0.53 to 30.3)		*2.92 (1.75 to 4.88)*
Any health insurance		1.20 (0.57 to 2.52)		*1.72 (1.09 to 2.69)*
Race/ethnicity				
White/Caucasian		Ref		Ref
Hispanic/Latino		2.42 (0.98 to 5.99)		0.97 (0.51 to 1.83)
African American		*4.40 (1.20 to 16.1)*		1.02 (0.40 to 2.60)
Asian		NA		1.43 (0.60 to 3.40)
Other		NA		0.99 (0.33 to 2.90)
History of homelessness		0.79 (0.57 to 2.52)		0.53 (0.14 to 1.93)
History of sex work		0.85 (0.09 to 7.84)		0.65 (0.14 to 2.90)
Depression at time of PEP		0.89 (0.38 to 2.10)		1.21 (0.76 to 1.94)
Anxiety at time of PEP		1.02 (0.43 to 2.43)		0.91 (0.56 to 1.48)
ADHD at time of PEP		0.54 (0.13 to 2.34)		1.72 (0.94 to 3.17)
Bipolar I/II at time of PEP		NA		1.35 (0.54 to 3.38)
Year of 1st NPEP Prescription		NA		*0.92 (0.87 to 0.96)*

Abbreviations: HR: Hazards Ratio (for Cox models); OR: Odds Ratio (for logistic models); aHR: adjusted Hazards Ratio (for multivariable Cox models); aOR: adjusted Odds Ratio (for multivariable logistic models); CI: confidence interval; Italics indicates statistical significance (P<0.05)

[1] Cox proportional hazards model

[2] Logistic regression model

Table 4

Association between documented crystal methamphetamine dependence and crystal meth use in the context of the exposure that led to NPEP visit and NPEP visit-level variables

	Unprotected Anal Intercourse[1]		Unprotected Receptive Anal Intercourse[1,2]		Known HIV infected partner[1]		Three-drug regimen[1]	
	***Bivariate* OR (95% CI)**	***Multivariable* aOR (95% CI)**	***Bivariate* OR (95% CI)**	***Multivariable* aOR (95% CI)**	***Bivariate* OR (95% CI)**	***Multivariable* aOR (95% CI)**	***Bivariate* OR (95% CI)**	***Multivariable* aOR (95% CI)**
CM use during exposure	***4.00 (1.90 to 8.40)***	***3.04 (1.37 to 6.79)***	***3.58 (1.90 to 6.78)***	***2.98 (1.55 to 5.75)***	**1.53 (0.97 to 2.44)**	**1.29 (0.77 to 2.15)**	***2.40 (1.47 to 3.90)***	***2.00 (1.16 to 3.45)***
CM dependence[3]	***2.38 (1.38 to 4.11)***	***2.25 (1.23 to 4.12)***	***2.66 (1.47 to 4.83)***	***1.98 (1.04 to 3.78)***	***2.03 (1.31 to 3.14)***	***2.26 (1.41 to 3.64)***	***2.68 (1.65 to 4.37)***	***3.27 (1.94 to 5.50)***
Age at first PEP visit		1.00 (1.00 to 1.00)		1.00 (1.00 to 1.00)		1.00 (1.00 to 1.00)		1.00 (1.00 to 1.00)
In primary care at Fenway Health		0.78 (0.55 to 1.10)		1.23 (0.80 to 1.90)		1.02 (0.73 to 1.43)		1.00 (0.72 to 1.40)
Any health insurance		1.09 (0.79 to 1.52)		0.84 (0.56 to 1.27)		0.95 (0.70 to 1.30)		1.02 (0.75 to 1.39)
Race/ethnicity								
White/Caucasian		Ref		Ref		Ref		Ref
Hispanic/Latino		0.69 (0.44 to 1.10)		0.80 (0.43 to 1.47)		1.30 (0.83 to 2.03)		*1.83 (1.16 to 2.91)*
African American		0.89 (0.47 to 1.68)		*0.37 (0.16 to 0.85)*		*1.89 (1.03 to 3.46)*		1.36 (0.73 to 2.54)
Asian		0.96 (0.48 to 1.92)		0.86 (0.38 to 1.94)		0.54 (0.26 to 1.13)		0.82 (0.42 to 1.62)
Other		1.21 (0.59 to 2.50)		0.65 (0.28 to 1.51)		0.92 (0.47 to 1.81)		1.48 (0.75 to 2.91)
History of homelessness		0.33 (0.12 to 0.96)		0.73 (0.16 to 3.31)		*3.11 (1.12 to 8.67)*		2.03 (0.66 to 6.24)
History of sex work		1.55 (0.38 to 6.33)		1.27 (0.26 to 6.07)		1.63 (0.56 to 4.75)		1.20 (0.38 to 3.74)
Depression at time of PEP		1.30 (0.87 to 1.94)		1.55 (0.98 to 2.44)		0.70 (0.49 to 1.01)		1.28 (0.89 to 1.83)
Anxiety at time of PEP		1.45 (0.96 to 2.19)		1.15 (0.71 to 1.85)		1.04 (0.71 to 1.51)		0.89 (0.61 to 1.30)
ADHD at time of PEP		*1.82 (1.01 to 3.27)*		1.18 (0.65 to 2.14)		0.65 (0.39 to 1.10)		0.90 (0.55 to 1.49)
Bipolar I/II at time of PEP		0.61 (0.28 to 1.31)		3.01 (0.88 to 10.4)		1.08 (0.53 to 2.22)		0.65 (0.31 to 1.36)
Year of first NPEP Prescription		1.03 (1.00 to 1.31)		0.98 (0.94 to 1.02)		0.99 (0.96 to 1.03)		*0.90 (0.87 to 0.93)*

Abbreviations: CM: crystal methamphetamine; OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval; NPEP: non-occupational post-exposure prophylaxis; Italics indicates statistical significance (P<0.05)

[1] Logistic generalized estimating equation model

[2] Restricted to patients reporting unprotected anal intercourse as the source of their exposure

[3]Estimated from a model that does not include CM use during exposure