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Abstract

Background: Treatment as Prevention (TasP) leading to increased HIV treatment optimism among men who have sex with men (MSM) has been previously associated with behavioural risk compensation, though not yet via crystal methamphetamine (CM) use. Among HIV-negative MSM in a TasP environment, this study aimed to investigate the prevalence of recent CM use over time, examine the association between HIV treatment optimism and CM use and initiation, and identify correlates of recent CM use and predictors of CM initiation.

Methods: Using data from a prospective behavioural cohort study of sexually-active MSM in the Vancouver area, we used multi-level generalized mixed effect models to evaluate temporal trends in CM use, univariable and multivariable logistic regression to identify covariates of recent CM use, and univariable and multivariable survival analysis to identify predictors of CM initiation.

Results: Of 497 HIV-negative cohort participants, 10.3% reported any recent CM use at enrollment. From 2012-2016, there were no statistically significant temporal trends in overall CM use or with routes of administration. In multivariable logistic regression analyses, HIV treatment optimism was not associated with recent CM use (not retained in final model) or CM initiation (aHR=1.06, 95% CI:0.98-1.15). Significant correlates of CM use include recent gamma-hydroxybutyrate (GHB) and ecstasy use, and having received/given drugs for sex.

Conclusions: Among HIV-negative MSM in Vancouver, HIV treatment optimism does not appear to be independently associated with CM use or initiation of use, though use of CM was both prevalent and stable over time.

Keywords: HIV/AIDS; methamphetamine; men who have sex with men (MSM); gay and bisexual men; HIV treatment optimism; treatment as prevention (TasP)

1. Introduction

Treatment as Prevention (TasP) involves the use of highly active antiretroviral therapy (HAART) to treat individual HIV infections as well as to impede transmission and prevent new infections in the larger population, a novel utility demonstrated by recent research (Lima et al., 2015; Lima et al., 2010; Rodger et al., 2016; WHO, 2012). This promise of HIV treatment success has contributed to reassurance with respect to HIV among men who have sex with men (MSM), termed "HIV treatment optimism". However, while recent research has shown that increased HIV treatment optimism was not accompanied by more frequent reports of high-risk sexual behavior (HRSB) among HIV-negative MSM (Moore et al., 2017), elsewhere, this optimism has been positively associated with HRSB (Brennan et al., 2010; Chen, 2013), predominantly characterized as condomless sex (Chen, 2012). Greater HIV treatment optimism has also been associated with not having education about HIV and HIV-positive serostatus (Macapagal et al., 2017).

Crystal methamphetamine (CM), a synthetic and potent psychostimulant, has been minimally investigated as an HRSB related to HIV treatment optimism. Prevalence of CM use has been well demonstrated to be substantially higher among MSM than the general population (Hunter et al., 2014; Lyons et al., 2013; Solomon et al., 2012). Use of CM results in heightened sexual desire and stamina, as well as lowered inhibitions (Vearrier et al., 2012). Consequently, CM has been associated with HRSB, including condomless anal intercourse and increased number of male partners, as well as more self-reported bacterial sexually transmitted infections (STIs) (Forrest et al., 2010; Hoenigl et al., 2016; Melendez-Torres et al., 2016b; Pantalone et al., 2014) and increased risk of HIV acquisition (Freeman et al., 2011; Hoenigl et al., 2016;

Melendez-Torres et al., 2016b; Plankey et al., 2007; Rajasingham et al., 2012; Vosburgh et al., 2012).

We could identify no previous research that has explored CM use among MSM in an environment where TasP has been heavily promoted. Numerous other factors have been shown to be associated with CM use among MSM, including concurrent use of other substances including erectile dysfunction drugs (EDDs), gamma-hydroxybutyrate (GHB), and amyl nitrites (poppers), as well as alcohol consumption, depression, older age, HIV positive serostatus, sex in public venues, transactional sex, previous STI diagnosis, being single, and engaging in objectively HRSB (Lea et al., 2016; Lyons et al., 2013; Melendez-Torres et al., 2016a; Mimiaga et al., 2010; Ober et al., 2009; Rhodes et al., 2007). Initiation of CM use has been investigated with qualitative work among MSM, demonstrating it to have taken place predominantly in a social, non-sexual setting, with limited knowledge of the drug (Parsons et al., 2007). To our knowledge, only a single study has examined the relationship between HIV treatment optimism and CM use, and though it concluded a significant negative association, was limited to a relatively small study sample of 197 black MSM in Boston, Massachusetts, in 2008 (Mimiaga et al., 2010). No study could be identified that investigated HIV treatment optimism as a predictor or correlate of initiation of CM use among MSM or otherwise. We believe this to be a significant dearth of knowledge of real potential public health consequence.

British Columbia's Seek and Treat for Optimal Prevention of HIV/AIDS (STOP HIV/AIDS) program has embraced a TasP strategy by expanding access to HIV testing, care, and treatment (i.e., HAART) as a pilot program in Vancouver since 2010 (BCCfE, 2017a, b; Heath et al., 2014; Ministry of Health, 2012). Given evidence supporting an association between TasP and HRSB (Brennan et al., 2010; Chen, 2013; Lachowsky et al., 2016b; Roth et al., 2017), and ample

evidence of the association between CM use and HRSB (Rajasingham et al., 2012; Vosburgh et al., 2012), this study aimed to examine the association between HIV treatment optimism and use and initiation of CM, investigate the prevalence of recent CM use from 2012 to 2016, and identify correlates of recent CM use and predictors of CM initiation, among HIV-negative MSM in a TasP environment. We hypothesized that HIV treatment optimism would be positively associated with CM use and a predictor of initiation of CM use.

2. Methods

2.1. Study Design and Participants

Data were drawn from the Momentum Health Study, a bio-behavioural, longitudinal study of MSM in Vancouver, Canada. Participants were recruited through respondent-driven sampling (RDS) from February 2012 to February 2015. With RDS, the sampling process is started by purposely selecting specific participants from the community as "seeds", who then initiate chains of peer referrals. Participants were given up to 6 coupons and encouraged to recruit from members of their social and sexual networks (Lachowsky et al., 2016a). Eligibility criteria included: being 16 years or older, gender identifying as a man, reporting sex with another man in the past 6 months, currently living in Metro Vancouver, and being able to complete the questionnaire in English. Attainment of written informed consent was followed by a 90-minute computer-assisted self-interview (CASI), which collected information on sociodemographic, psychosocial, and behavioural factors. Lastly, a nurse-administered questionnaire included clinical STI/HIV screening and questions regarding history of STI and mental health diagnoses. Participants were given the option to consent to a longitudinal cohort, with study visits every 6 months up to a maximum of 4 years. Compensation consisted of a CAD 50 honorarium for each study visit and an additional CAD 10 for each subsequent participant recruited. Approval was

granted by the Research Ethics Boards of The University of British Columbia, The University of Victoria, and Simon Fraser University. Data from February 2012 to February 2016 were included in this analysis.

2.2 Dependent Variable

The primary outcome of this analysis was any CM use in the six-months prior to a study visit. During the CASI, participants were asked "In the PAST 6 MONTHS have you used Crystal Methamphetamine ('Crystal', 'meth')" with dichotomous "No" or "Yes" response options. Those who selected "Yes" were asked to specify the number of days they used CM in the past six-months.

The secondary outcome of this analysis was first-reported-use of CM among participants who had not previously reported CM use in the study. First-reported-use of CM was the event of interest in our survival analysis; thus a "failure" in the survival analysis was defined as the first report of CM usage for participants with no CM use reported at any previous study visit.

2.3. Independent Variables

All data for explanatory variables were collected during the CASI. Demographic information included age, sexual orientation, ethnicity, and relationship status.

Psychosocial factors were measured with several scales:

2.3.1. HIV Treatment Optimism-Skepticism Scale. A 12-item scale, where higher scores indicate greater optimism (score range: 0-36; α=0.84). Using a 4-point Likert scale from "Strongly Disagree" to "Strongly Agree", participants provided their level of agreement with items aimed at assessing their attitudes toward HIV treatment in terms of reducing the likelihood and consequence of HIV (e.g., "If every HIV-positive person took the new treatments, the AIDS epidemic would be over." (Van de Ven et al., 2000).

2.3.2. Escape Motivation Scale. A 12-item scale, with greater scores indicating more escape motivations (score range: 12-48; study α=0.90). Using a 4-point Likert scale from "Strongly Disagree" to "Strongly Agree", participants provided their level of agreement with items aimed at assessing how much being under the influence of one or more substances might be related to sexual risk taking (e.g., "When I am high or drunk, I am more likely to do sexual things I usually wouldn't do." (McKirnan et al., 2001).

2.3.3. Gay/Bisexual Self-Esteem. A 7-item scale, reverse-coded, with higher scores indicating lower self-esteem (score range: 0-21; study α=0.90). Using a 4-point Likert scale from "Strongly Agree" to "Strongly Disagree", participants provided their level of agreement with items aimed at assessing their self-esteem as a gay/bisexual man (e.g., "I feel that I am a person of worth, at least on an equal basis with others." (Herek and Glunt, 1995).

2.3.4. Hospital Anxiety and Depression Scale. Two 7-item subscales, with greater scores indicating more anxiety and depression symptomology (score range: 0-21 for each; study α=0.86 and α=0.81, respectively). Using various 4-point scales, participants provided responses to items aimed at assessing anxiety and depression (e.g., "I get a sort of frightened feeling as if something awful is about to happen", and "I have lost interest in my appearance", respectively (Snaith, 2003; Whelan-Goodinson et al., 2009; Zigmond and Snaith, 1983).

Factors pertaining to HIV prevention and risk reduction strategies addressed recent (past 6 months [P6M]) consistent and selective condom use, sero-sorting, sero-positioning, "viral load sorting", and self-perceived current risk of acquiring HIV. Sexual history and practices over the P6M were investigated through questions addressing number of male sex partners, use of the internet or mobile apps to seek sex, any escort work, anal sex role preferences, group sex participation, and any recent STI diagnosis. Lastly, P6M substance use was probed by inquiring

about having received or given drugs for sex, binge drinking (defined as 5+ drinks on one occasion), and use of EDDs, poppers, GHB, and ecstasy.

2.4. Statistical Analysis

We conducted baseline descriptive statistics for HIV-negative participants who enrolled in the cohort. To account for the potential interdependence of these observations arising from their longitudinal nature, three-level generalized linear mixed modelling with an unstructured covariance matrix for the random effects, accounting for RDS recruitment chain and respondents' multiple visits, was used (i.e., study visit within participant within RDS recruitment chain). We used random intercept modelling to account for interdependence among responses within clusters. The estimated effect of a time-dependent predictor is considered as a combination of the effect of varying predictor values within clusters, and the effect of varying predictor values between clusters. Time-independent predictors only have between-cluster variations. Only sexual orientation and ethnicity were treated as time-independent. A temporal trend was assessed using logistic regression with recent CM use as the dependent variable and time, included as six-month periods, as the independent variable. Factors associated with recent CM use were assessed using multivariable logistic regression. Model selections were conducted using a backward elimination technique based on two criteria (Akaike Information Criterion [AIC] and type III p-values). The variable with the highest Type III p-value was dropped at each step of the selection process until the final model reached the optimum (minimum) AIC. We performed univariable survival analysis to identify predictors of crystal methamphetamine initiation and subsequently built a multivariable confounder model with HIV treatment optimism forced into the model to assess our hypothesis. The Cox proportional hazard models used the robust sandwich covariance matrix for the within-participant correlation. For multivariable

models, missing data in continuous variables was imputed with the median of the observed data (percentage of missing in continuous variables was < 5%). Observations with missing data in categorical variables were removed from the analyses and the final number of observations used in the multivariable models were 2144 out of 2170 (98.8%) for the recent CM use analysis, and 1420 out of 1476 (96.2%) for the CM initiation analysis. All statistical tests were two-sided and considered significant at $\alpha < 0.05$. All analyses in this study were conducted using SAS® versions 9.4 (SAS, North Carolina, United States).

3. Results

3.1. Descriptive Characteristics of Study Population at Enrollment

A total of 774 participants were recruited from February 2012 to February 2015, of whom 698 consented to be included into the prospective cohort. Of the cohort participants, 497 (71.2%) tested HIV-negative at the initial study visit, comprising our study sample for the longitudinal logistic regression analysis of CM use. Of these participants, 413 (83.1%) returned for at least one follow-up visit, of which 377 (91.3%) had no reported use of CM at enrollment, comprising our study sample for our survival analysis of CM initiation.

Descriptive statistics of the study sample at enrollment are shown in Table 1. At enrollment, 10.3% of HIV-negative MSM reported any CM use in the previous six-months. Among these, the routes of administration were: 70.6% smoking, 60.8% snorting, 25.5% injecting, and 17.7% hooping. Of those who reported any use, 58.8% used less than monthly, 11.8% used monthly, 13.7% used weekly, 5.9% used more than weekly, and 9.8% used daily or almost daily.

There was no statistically significant temporal trend in overall CM use during the study period from 2012 to 2016 (p=0.179), (see supplementary material[1]), nor with any of the listed routes of administration: smoking (p=0.535), snorting (p=0.282), hooping (p=0.278), and injecting (p=0.301).

CM use did not differ by follow-up time or retention in the cohort. 20.5% of individuals reporting CM use at least once did not complete any further visits (were lost to follow up) compared with 16.2% of those who reported no CM use during the study period (p=0.340). Further, there was no difference in median follow-up time between those who never reported CM use (2.3 years) compared with the median follow-up time among those who reported any CM use (2.0 years, p=0.170). Among the 413 participants who returned for at least one follow-up visit, the median number of visits was 5.

Bivariate analysis and univariable associations of correlates of recent CM use are shown in Table 2, while Table 3 provides the variables that were selected for our final multivariable regression analysis.

Of the 377 participants who reported no recent CM use at enrollment and who completed at least one follow-up visit, 32 (8.5%) initiated CM use over the course of the study. The incidence rate (IR) was 3.85 per 100 person-years (95% CI: 2.72-5.45). Bivariate analysis and univariable associations comparing variables of interest between study visits indicating first use of CM and study visits with no previous CM use are reported in Table 4.

A multivariable confounder model examining the association between HIV treatment optimism and CM initiation was constructed with consideration of sexual orientation, escape

[1] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:…

motive scale, group sex participation, and escort work as confounders. The final confounder model is illustrated in Table 5.

4. Discussion

In Vancouver, British Columbia, Treatment as Prevention has been policy as the STOP HIV/AIDS program since 2010 (BCCfE, 2017a, b; Heath et al., 2014; Ministry of Health, 2012). In seeking to explore the relationship between TasP and its associated HIV treatment optimism among HIV-negative MSM, we examined if optimism was associated with both recent CM use and initiation of CM use. Results of the study suggest that HIV treatment optimism is associated with both ongoing CM use and initiation of its use, but this association is no longer statistically significant after accounting for other important factors.

Analysis of the temporal trend of CM use over the 4-year time period did not reveal any statistically significant changes. This apparent stability appears to be inconsistent with global trends of amphetamine use as well as Canadian crime statistics, both of which report increases in CM activity (Statistics Canada, 2016; UNODC, 2017). However, among HIV-negative or unknown status MSM from 2010 to 2014, Lea et al. (2016) found no trend with regular CM use but did note an increase (8.4% to 9.9%) with any CM use over the same time period among HIV-negative MSM, comparable to our prevalence of 10.3%. However, this study had a significantly larger sample (70,732 participants).

Higher escape motivation scale scores were significantly associated with both CM use and CM initiation in our multivariable models. We postulate that individuals partake in initiation and use of CM to facilitate “escape” from inhibition brought about by fear of HIV acquisition, to which the scale pertains (McKirnan et al., 2001). This aligns with previous research by McKirnan et al. (1996), where it was proposed that individuals “use substances strategically to

induce a state of cognitive escape regarding personal risk" (McKirnan et al., 1996). Further, it is hypothesized that such an escape contributes to indices of HRSB as shown in univariable associations, namely increased number of anal sex partners, group sex participation, increased likelihood of recent STI diagnosis, and condomless anal sex with an serodiscordant or unknown serostatus partner. We conjecture CM use to be a mediator between this escape motivation and these HRSB, thus their significance as correlates of recent CM use and CM initiation in our multivariable models.

Our final multivariable model of recent CM use included recent GHB and ecstasy use as correlates, consistent with previous literature revealing use of other illicit drugs as a significant risk factor for CM use (Herman-Stahl et al., 2006, 2007; Iritani et al., 2007; Lea et al., 2016; Lyons et al., 2013). This further demonstrates that CM use is not isolated from use of other substances, especially those typically associated with sex and HRSB, such as GHB (Daskalopoulou et al., 2014; Mimiaga et al., 2015; Mimiaga et al., 2008; Sewell et al., 2017; Stall et al., 2003). It is also noteworthy that both having given and received drugs for sex were also risk factors retained in our final model, concurring with previous research (Koken et al., 2005; Ober et al., 2009; Viswanath et al., 2017). However, MSM who reported having previously engaged in escort work (predating the six-month recall window at enrollment) were less likely to report current CM use; this result was not seen for recent escort work. Previous research has demonstrated significantly higher prevalence of CM use among MSM populations engaged in escort work compared to those not engaged (Grov et al., 2014; Mimiaga et al., 2009). We postulate that the negative association between former escort work and CM use seen in the final multivariable model may be a consequence of unmeasured factors simultaneously influencing an individual away from both escort work and CM use.

Those using CM in our study population reported several objective indicators of increased risk of HIV acquisition at the univariable or multivariable level, including decreased odds of consistent condom use, an increased number of anal sexual partners, and increased likelihood of attending a group sex event, participating in condomless anal sex with a serodiscordant/unknown status partner, and having had a recently diagnosed STI (Freeman et al., 2011; Hoenigl et al., 2016; Melendez-Torres et al., 2016b; Rajasingham et al., 2012; Vearrier et al., 2012; Vosburgh et al., 2012). Despite the presence of these established risk factors, in 120 of 171 study visits (70.2%), MSM using CM rated their current risk of HIV acquisition as "low". It is possible that those engaging in CM use and these associated risk behaviors do not subjectively perceive the link between these behaviors and the increased risk of HIV acquisition. Use of HIV pre-exposure prophylaxis (PrEP) might have been a plausible explanation to account for this perceived lack of risk; however, PrEP use was only reported at 12 study visits and concurrently with recent use of CM at a single study visit.

Our study is not without limitations. Given the longitudinal nature of our analysis, we were unable to use RDS-weighting to account for the violation of non-independence of data; instead we did so by using multi-level modeling. Some of the confidence intervals from our multivariable models are wide, potentially as a consequence of few observations within levels of our independent variables. These estimates may be hindered by reporting and social desirability biases; nevertheless, we reason that the financial incentive and privacy of a CASI effectively mitigated and minimized these threats. We aimed to reduce recall bias by asking participants about the previous six-months; we do not suspect differential recall between those reporting CM use and those not reporting use. We also used an arguably broad definition of CM users, in that

there may be hidden but significant differences between regular users and occasional users, as prior research has explored (Lea et al., 2016).

The results of our study present a number of public health implications. First, HIV-negative MSM appear to use or begin to use CM independently of current TasP policy and health promotion efforts, providing reassurance, at least in this context, to those concerned with respect to risk compensation in terms of substance use associated with these efforts. Second, our analysis informs us that CM use and its implications remain a persistent public health challenge. Third, HIV-negative MSM who use CM appear to be subjectively evaluating themselves at low-risk despite the objective high-risk indicators for HIV acquisition of their sexual behavior. Prospective public health education could highlight the risks associated with CM, potentially highlighting associations between CM use and poor treatment adherence and resultant unsuppressed viral load among HIV-positive MSM (Feldman et al., 2015; Hinkin et al., 2007; Skeer et al., 2012).

5. Conclusion

Among HIV-negative MSM in Vancouver, HIV treatment optimism associated with TasP does not appear to be independently associated with CM use or initiation of use, though use of CM was both prevalent and stable over time. CM use is associated with use of other substances, contributing to evidence of poly-substance use within a syndemic framework for HIV risk. As with prior research, giving or receiving drugs in exchange for sex was also associated with CM use. Most concerning was the clear majority of CM-using participants perceiving low current HIV risk despite reporting HRSB objectively. Therefore, renewed population-specific interventions and health promotion efforts are urgently needed.

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Table 1: Descriptive statistics of study sample at enrollment (N = 497).

	n or (median)	% or (Q1, Q3)
Demographics		
Age	(30)	(24, 39)
Sexual Orientation		
Gay	427	85.9
Bisexual/Other	70	14.1
Race/Ethnicity		
White	370	74.5
Asian	56	11.3
Indigenous	23	4.6
Other	48	9.7
Relationship Status		
Single	301	60.6
Partnered/Married	196	39.4
HIV Prevention Practices and Factors		
Self-Perceived Current Risk of Acquiring HIV		
Low	444	89.3
High	53	10.7
Sexual History and Practices		
Number of Anal Sex Partners in P6M	(3)	(1, 7)
Escort Work		
No	434	87.4
Yes, in P6M	28	5.6
Yes, not in P6M	35	7.0
Anal Sex over P6M		
No anal sex	63	12.9
Only condom-protected	121	24.9
Any condomless, but only seroconcordant	129	26.5
Any condomless, including unknown status or serodiscordant partner	174	35.7
Participated in Group Sex in P6M	114	22.9
Diagnosis of any STI in P6M	43	9.0
Alcohol and Substance Use		
Received Drugs for Sex		
No	443	89.2
Yes, in P6M	23	4.6
Yes, not in P6M	31	6.2
Gave Drugs for Sex		
Yes, in P6M	480	96.6
Yes, in P6M	9	1.8
Yes, not in P6M	8	1.6
Binge Drinking Frequency		
Monthly or less	367	74.0
Weekly/Daily or almost daily	129	26.0
Used EDDs in P6M	81	16.3

Used Poppers in P6M	158	31.8
Used GHB in P6M	65	13.1
Used Ecstasy in P6M	127	25.6

Q1, Q3 = first quartile, third quartile values; P6M = past 6 months; STI = sexually transmitted infection; EDDs = erectile dysfunction drugs; GHB = gamma hydroxybutyrat

Table 2: Descriptive statistics and univariable associations with crystal methamphetamine use over the past 6 months (P6M) versus no use. All cohort participant visits (N = 2170).

	No CM use P6M		Used CM P6M		Univariable		
	n or (median)	% or (Q1, Q3)	n or (median)	% or (Q1, Q3)	OR	95% CI	
Demographics							
Age	(31)	(26, 41)	(33)	(26, 41)	1.00	0.97	1.02
Sexual Orientation							
Gay	1730	93.6	118	6.4	Ref		
Bisexual/Other	269	83.5	53	16.5	**2.75**	**1.54**	**4.91**
Race/Ethnicity							
White	1521	92.9	117	7.1	Ref		
Asian	246	97.6	6	2.4	**0.26**	**0.07**	**0.94**
Indigenous	72	67.9	34	32.1	**6.64**	**2.44**	**18.11**
Other	160	92.0	14	8.0	1.28	0.52	3.19
Relationship Status							
Single	1073	91.4	101	8.6	Ref		
Partnered/Married	926	93.0	70	7.0	**0.62**	**0.39**	**0.98**
Self-Perceived Current Health							
Excellent/Very good	1151	95.0	60	5.0	Ref		
Good	644	88.8	81	11.2	**2.26**	**1.39**	**3.67**
Fair/Poor	203	87.1	30	12.9	**2.51**	**1.25**	**5.07**
Psychosocial Factors and Scales							
HIV Optimism Scale (α=0.84)	(25)	(22, 28)	(27)	(25, 31)	**1.07**	**1.02**	**1.13**
Escape Motivation Scale (α=0.90)	(28)	(24, 32)	(32)	(28, 36)	**1.12**	**1.08**	**1.17**
Self-Esteem Scale (α=0.90)	(7)	(3, 9)	(8)	(5, 10)	**1.07**	**1.01**	**1.13**
HADS Anxiety Sub-Scale (α=0.86)	(7)	(4, 10)	(9)	(7, 12)	**1.10**	**1.03**	**1.16**
HADS Depression Sub-Scale (α=0.81)	(3)	(1, 6)	(4)	(2, 8)	**1.09**	**1.02**	**1.17**
HIV Prevention Practices and Factors							
Consistent Condom Use (Ref: No)	1211	95.2	61	4.8	**0.41**	**0.26**	**0.65**
Sero-position for Anal Sex (Ref: No)	560	91.1	55	8.9	1.34	0.81	2.21
Sero-sort for Anal Sex (Ref: No)	786	92.6	63	7.4	1.19	0.75	1.89
Viral Load sort for Anal Sex (Ref: No)	199	77.4	58	22.6	**4.64**	**2.64**	**8.18**
Self-Perceived Current Risk of Acquiring HIV							

Low	1888	94.0	120	6.0	Ref		
High	111	68.5	51	31.5	**6.23**	**3.45**	**11.25**
Sexual History and Practices							
Number of Anal Sex Partners in P6M	(2)	(1, 5)	(4)	(1, 15)	**1.03**	**1.01**	**1.04**
Used Internet to Seek Sex							
Not in the past 6 months	1069	95.3	53	4.7	Ref		
Less than once per month	329	90.1	36	9.9	1.82	0.99	3.34
About once per month	167	87.0	25	13.0	**2.19**	**1.06**	**4.52**
More than once per month	432	88.3	57	11.7	**3.52**	**2.04**	**6.07**
Escort Work							
No	1775	93.5	124	6.5	Ref		
Yes, in P6M	45	59.2	31	40.8	**12.08**	**5.15**	**28.32**
Yes, not in P6M	179	91.8	16	8.2	1.37	0.58	3.23
Anal Sex over P6M							
Any condomless, but only seroconcordant	601	95.7	27	4.3	Ref		
No anal sex	382	94.6	22	5.4	0.90	0.40	2.03
Only condom-protected	443	96.3	17	3.7	0.82	0.37	1.83
Any condomless, including unknown status or serodiscordant partner	551	84.3	103	15.7	**3.93**	**2.16**	**7.15**
Participated in Group Sex in P6M (Ref: No)	335	86.3	53	13.7	**2.57**	**1.55**	**4.25**
Diagnosis of any STI in P6M (Ref: No)	124	84.9	22	15.1	**2.52**	**1.28**	**4.98**
Alcohol and Substance Use							
Received Drugs for Sex							
No	1843	95.3	90	4.7	Ref		
Yes, in P6M	21	36.2	37	63.8	**47.11**	**19.70**	**112.67**
Yes, not in P6M	135	75.4	44	24.6	**7.07**	**3.42**	**14.61**
Gave Drugs for Sex							
No	1931	92.9	147	7.1	Ref		
Yes, in P6M	9	40.9	13	59.1	**27.06**	**6.67**	**109.86**
Yes, not in P6M	58	84.1	11	15.9	2.22	0.61	8.05
Binge Drinking Frequency							
Monthly or less	1570	92.5	127	7.5	Ref		
Weekly/Daily or almost daily	417	90.7	43	9.3	1.33	0.79	2.27
Used EDDs in P6M (Ref: No)	263	77.1	78	22.9	**6.04**	**3.61**	**10.10**

Used Poppers in P6M (Ref: No)	490	83.6	96	16.4	**4.43**	**2.76**	**7.12**
Used GHB in P6M (Ref: No)	132	57.4	98	42.6	**21.31**	**12.35**	**36.79**
Used Ecstasy in P6M (Ref: No)	445	82.0	98	18.0	**5.67**	**3.46**	**9.28**

Q1, Q3 = first quartile, third quartile values; 95% CI = 95% confidence interval; HADS = Hospital Anxiety and Depression Scale; P6M = past 6 months; STI = sexually transmitted infection; EDDs = erectile dysfunction drugs; GHB = gamma hydroxybutyrate; Data with **bold emphasis** indicates statistical significance at $P < 0.05$.

Table 3: Final multivariable model of factors associated with crystal methamphetamine use over the past 6 months (P6M) versus no use. All cohort participant visits (N = 2144).

	Multivariable Model		
	aOR	**95% CI**	
Demographics			
Age	**1.04**	**1.00**	**1.07**
Sexual Orientation (Ref: Gay)			
Bisexual/Other	**4.33**	**2.15**	**8.71**
Race/Ethnicity (Ref: White)			
Asian	0.51	0.08	3.19
Indigenous	**10.04**	**3.20**	**31.47**
Other	1.67	0.59	4.68
Current Health (Ref: Excellent/Very Good)			
Good	**2.20**	**1.20**	**4.05**
Fair/Poor	1.57	0.62	3.94
Psychosocial Factors and Scales			
Escape Motivation Scale (α=0.90)	**1.06**	**1.01**	**1.12**
HADS Anxiety Sub-Scale (α=0.86)	**1.09**	**1.02**	**1.18**
HIV Prevention Practices and Factors			
Consistent Condom Use (Ref: No)	**0.41**	**0.23**	**0.74**
Sero-position for Anal Sex (Ref: No)	**3.61**	**1.84**	**7.09**
Sexual History and Practices			
Escort Work (Ref: No)			
Yes, in P6M	1.69	0.57	4.95
Yes, not in P6M	**0.31**	**0.11**	**0.91**
Diagnosis of any STI in P6M (Ref: No)	2.36	0.98	5.70
Alcohol and Substance Use			
Received Drugs for Sex (Ref: No)			
Yes, in P6M	**11.66**	**3.75**	**36.29**
Yes, not in P6M	**4.39**	**1.75**	**11.01**
Gave Drugs for Sex (Ref: No)			
Yes, in P6M	**5.61**	**1.05**	**29.89**
Yes, not in P6M	0.85	0.21	3.51
Used GHB in P6M (Ref: No)	**9.80**	**5.09**	**18.86**
Used Ecstasy in P6M (Ref: No)	**2.98**	**1.56**	**5.68**

95% CI = 95% confidence interval; HADS = Hospital Anxiety and Depression Scale; P6M = past 6 months; STI = sexually transmitted infection; GHB = gamma hydroxybutyrate; Data with **bold emphasis** indicates statistical significance at $P < 0.05$.

Table 4: Descriptive statistics and univariable associations with initiation of crystal methamphetamine use over the past 6 months (P6M) versus no previously reported use. Last visit included for descriptive statistics (N=377). All cohort participant visits until first reported CM use for survival analysis (N = 1476).

	No reported use of CM		First use of CM after baseline		Univariable		
	n or (median)	% or (Q1, Q3)	n or (median)	% or (Q1, Q3)	HR	95% CI	
Demographics							
Age	(31)	(27, 42)	(32.5)	(26, 40)	0.99	0.96	1.02
Sexual Orientation							
Gay	291	93.6	20	6.4	Ref		
Bisexual/Other	54	81.8	12	18.2	**3.49**	**1.71**	**7.15**
Race/Ethnicity							
White	255	91.4	24	8.6	Ref		
Asian	47	97.9	1	2.1	0.25	0.03	1.85
Indigenous	11	84.6	2	15.4	1.76	0.41	7.44
Other	32	86.5	5	13.5	1.92	0.73	5.03
Relationship Status							
Single	174	89.2	21	10.8	Ref		
Partnered/Married	171	94.0	11	6.0	0.55	0.27	1.14
Self-Perceived Current Health							
Excellent/Very good	182	94.3	11	5.7	Ref		
Good	117	86.7	18	13.3	**2.88**	**1.36**	**6.09**
Fair/Poor	46	93.9	3	6.1	1.34	0.37	4.82
Psychosocial Factors and Scales							
HIV Optimism Scale (α=0.84)	(27)	(23, 29)	(27)	(25, 30)	**1.07**	**1.00**	**1.15**
Escape Motivation Scale (α=0.90)	(28)	(24, 31)	(31)	(27, 36)	**1.10**	**1.04**	**1.16**
Self-Esteem Scale (α=0.90)	(7)	(3, 9)	(9)	(6, 11)	**1.11**	**1.03**	**1.20**
HADS Anxiety Sub-Scale (α=0.86)	(7)	(4, 10)	(9)	(6, 11)	**1.08**	**1.00**	**1.17**
HADS Depression Sub-Scale (α=0.81)	(3)	(1, 6)	(4)	(2, 6)	1.02	0.93	1.13
HIV Prevention Practices and Factors							
Consistent Condom Use (Ref: No)	198	93.8	13	6.2	**0.42**	**0.21**	**0.84**
Sero-position for Anal Sex (Ref: No)	85	86.7	13	13.3	1.87	0.92	3.80
Sero-sort for Anal Sex (Ref: No)	142	93.4	10	6.6	0.67	0.32	1.41
Viral Load sort for Anal Sex (Ref: No)	34	75.6	11	24.4	**4.91**	**2.37**	**10.18**

Self-Perceived Current Risk of Acquiring HIV							
Low	324	92.8	25	7.2	Ref		
High	21	75.0	7	25.0	**4.89**	**2.11**	**11.31**
Sexual History and Practices							
Number of Anal Sex Partners in P6M	(2)	(1, 4)	(4.5)	(2, 15)	**1.01**	**1.01**	**1.02**
Used Internet to Seek Sex							
Not in the past 6 months	215	95.1	11	4.9	Ref		
Less than once per month	57	98.3	1	1.7	0.35	0.05	2.74
About once per month	16	80.0	4	20.0	3.06	0.97	9.66
More than once per month	56	77.8	16	22.2	**4.66**	**2.15**	**10.11**
Escort Work							
No	307	91.6	28	8.4	Ref		
Yes, in P6M	6	66.7	3	33.3	**5.05**	**1.53**	**16.68**
Yes, not in P6M	32	97.0	1	3.0	0.36	0.05	2.64
Anal Sex over P6M							
Any condomless, but only seroconcordant	114	94.2	7	5.8	Ref		
No anal sex	73	94.8	4	5.2	0.88	0.26	3.00
Only condom-protected	76	96.2	3	3.8	0.61	0.16	2.35
Any condomless, including unknown status or serodiscordant partner	81	82.7	17	17.3	**3.03**	**1.25**	**7.31**
Participated in Group Sex in P6M (Ref: No)	45	80.4	11	19.6	**2.72**	**1.31**	**5.65**
Diagnosis of any STI in P6M (Ref: No)	23	82.1	5	17.9	**3.23**	**1.24**	**8.45**
Alcohol and Substance Use							
Received Drugs for Sex							
No	315	92.1	27	7.9	Ref		
Yes, in P6M	6	66.7	3	33.3	**6.38**	**1.92**	**21.13**
Yes, not in P6M	24	92.3	2	7.7	1.15	0.27	4.84
Gave Drugs for Sex							
No	333	92.0	29	8.0	Ref		
Yes, in P6M	0	0.0	2	100.0	**13.26**	**3.05**	**57.59**
Yes, not in P6M	11	91.7	1	8.3	1.10	0.15	8.10
Binge Drinking Frequency							
Monthly or less	280	91.8	25	8.2	Ref		
Weekly/Daily or almost daily	61	89.7	7	10.3	1.14	0.49	2.65

Used EDDs in P6M (Ref: No)	47	78.3	13	21.7	**4.21**	**2.08**	**8.54**
Used Poppers in P6M (Ref: No)	71	78.9	19	21.1	**4.85**	**2.39**	**9.83**
Used GHB in P6M (Ref: No)	23	57.5	17	42.5	**18.07**	**9.00**	**36.27**
Used Ecstasy in P6M (Ref: No)	71	79.8	18	20.2	**4.38**	**2.17**	**8.84**

Q1, Q3 = first quartile, third quartile values; 95% CI = 95% confidence interval; HADS = Hospital Anxiety and Depression Scale; P6M = past 6 months; STI = sexually transmitted infection; EDDs = erectile dysfunction drugs; GHB = gamma hydroxybutyrate; Data with **bold emphasis** indicates statistical significance at $P < 0.05$.

Table 5: Final multivariable confounding model of factors associated with first reported use of crystal methamphetamine use over the past 6 months (P6M) versus no reported use throughout the study period with HIV Optimism Scale forced in. All cohort participant visits until first reported CM use for survival analysis (N = 1420).

	Multivariable Model		
	aHR	**95% CI**	
Demographics			
Sexual Orientation (Ref: Gay)			
Bisexual/Other	**3.96**	**1.91**	**8.21**
Psychosocial Factors and Scales			
HIV Optimism Scale (α=0.84)	1.06	0.98	1.15
Escape Motivation Scale (α=0.90)	**1.10**	**1.04**	**1.16**
Sexual History and Practices			
Escort Work (Ref: No)			
Yes, in P6M	**3.88**	**1.15**	**13.11**
Yes, not in P6M	0.20	0.03	1.47
Participated in Group Sex in P6M (Ref: No)			
Yes	2.01	0.93	4.34

95% CI = 95% confidence interval; P6M = past 6 months; Data with **bold emphasis** indicates statistical significance at P < 0.05.