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## Crystal Methamphetamine Injection Predicts Slower HIV RNA Suppression among Injection Drug Users

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### Abstract

We examined the impact of crystal methamphetamine injection on HIV RNA suppression among a prospective cohort of HIV-positive injection drug users initiating antiretroviral therapy. A multivariate Cox regression analysis found crystal methamphetamine injection to be negatively associated with viral load suppression (RH = 0.63 [95% CI: 0.40 – 0.98];  $p = 0.039$ ). This study is the first to our knowledge to demonstrate an association between crystal methamphetamine use and HIV RNA suppression.

### Keywords

methamphetamine; intravenous drug abuse; HIV; viral load

## 1. INTRODUCTION

Crystal methamphetamine, a powerful stimulant drug, has received considerable attention in recent years as reports of escalating drug production and consumption have surfaced globally (World Health Organization, 2010). Of particular concern is the relationship between crystal methamphetamine and HIV/AIDS. Use of crystal methamphetamine has been linked to sexual and parenteral risk behaviours and increased likelihood of HIV seroconversion, particularly among men who have sex with men (Kozlov et al., 2006; Kral et al., 2001).

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#### Contributors

Nadia Fairbairn and Evan Wood were responsible for the study design and prepared the first draft of the analysis. Ruth Zhang contributed to the study design and conducted the statistical analyses. M-J Milloy, Thomas Kerr and Julio Montaner contributed to the main content and provided critical comments on the final draft. All of the authors approved the final version submitted for publication.

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#### Conflict of interest

Julio Montaner has received grants from, has served as an ad hoc advisor to, and has spoken at various events sponsored by Abbott, Argos Therapeutics, Bioject Inc., Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Hoffmann-La Roche, Janssen-Ortho, Merck Frosst, Pfizer, Schering, Serono Inc., Thera Technologies, Tibotec and Trimeris. No competing interests declared by Nadia Fairbairn, Thomas Kerr, M-J Milloy, Ruth Zhang, or Evan Wood.

Previous studies also indicate that HIV-positive individuals who use crystal methamphetamine have poor adherence to antiretroviral therapy (Marquez et al., 2009). However, to our knowledge, the relationship between crystal methamphetamine use and the outcomes from antiretroviral therapy (ART) have not been well described. Given the substantial threat rising crystal methamphetamine use poses to HIV prevention and treatment strategies (Plankey et al., 2007), we conducted the present study to examine the association between crystal methamphetamine injection and HIV RNA suppression among a cohort of HIV-positive injection drug users (IDUs) initiating ART.

## 2. METHODS

The ACCESS cohort is an ongoing prospective study of HIV-positive injection drug-using individuals recruited through self-referral and street outreach from Vancouver's Downtown Eastside since May 1996, and has been described in detail previously (Strathdee et al., 1998). Briefly, at baseline participants provide a venous blood sample and complete an interviewer-administered questionnaire. Follow-up interviews are conducted semi-annually thereafter and participants are provided a nominal stipend at each study visit. The University of British Columbia's Research Ethics Board has annually provided ethical approval.

The primary endpoint in this analysis was time to viral load suppression to  $\leq 500$  copies/mL and use of injection crystal methamphetamine was the primary independent variable of interest. Additional drug use variables considered included: Frequent ( $\geq$  daily) heroin and cocaine injection and frequent crack cocaine smoking. We also considered gender, age ( $< 24$  years versus  $\geq 24$  years), ethnicity (Caucasian versus other), baseline viral load (per  $\log^{10}$ ) and baseline CD4 count (per 100 cells/ $\text{mm}^3$ ) as potential confounders. Variable definitions were consistent with previous analyses (Strathdee et al., 1998; Wood et al., 2004), and behavioral variables, including crystal methamphetamine injection, were treated as time updated covariates. The multivariate model was fit using an *a priori* defined model-building approach in which we adjusted for all variables that were statistically significant at the  $p < 0.05$  level in the bivariate analyses. All statistical analyses were performed using SPSS 12.0. All  $p$ -values are two sided.

## 3. RESULTS

Between September 1996 and April 2008, 384 (54.2%) antiretroviral-naïve patients initiated HAART among whom 163 (42.5%) were women and the median follow-up duration was 18 (inter-quartile range: 6 – 49). Overall, 36 (9.4%) reported crystal methamphetamine at any time during follow-up.

A multivariate Cox proportional hazards analysis examining factors independently associated with time to viral load suppression is shown in Table 1. As shown here, crystal methamphetamine injection (Relative Hazard = 0.63 [95% CI: 0.40 – 0.98];  $p = 0.039$ ), remained independently associated with a reduced rate of viral load suppression even after adjustment for age, baseline CD4 cell count and viral load, heroin injection and cocaine injection.

## 4. CONCLUSIONS

In the present study, we examined a cohort of HIV-positive IDUs initiating ART and observed that injection of crystal methamphetamine was independently and negatively associated with HIV viral load suppression. To our knowledge, this study is the first to demonstrate an association between crystal methamphetamine and reduced virological response to antiretroviral therapy.

Our findings are most likely explained by the fact that the psychopharmacological effects of crystal methamphetamine may undermine antiretroviral treatment adherence (Hinkin et al., 2007; Cho & Melega, 2002). Biological studies also indicate that methamphetamine may play a cofactor role in enhancing HIV infection and replication by promoting direct HIV infection of macrophages (Liang et al., 2008).

Though the present study has limitations inherent in all observational studies, these data contribute further evidence to the negative health outcomes associated with crystal methamphetamine use among HIV-positive individuals. Given the continued increases in crystal methamphetamine consumption despite attempts to deter use, strategies to improve drug treatment, as well as improved HIV prevention and treatment adherence strategies for this high-risk group require urgent implementation.

#### HIGHLIGHTS

- Crystal meth injection negatively associated with time to HIV RNA suppression
- First study to show association between crystal meth and virological response
- Further evidence for negative health outcomes of crystal meth in people with HIV

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**Table 1**

Multivariate Cox Regression analysis of factors independently associated with the time to HIV RNA suppression < 500 copies/mL

Variable	Adjusted <sup>**</sup> Relative Hazard (RH)	95% Confidence Interval (CI)	<i>p</i> - value
<b>Baseline CD4 Count</b>			
(Per 100 cells/mm <sup>3</sup> )	0.90	(0.84 – 0.96)	0.001
<b>Crystal Methamphetamine Injection</b>			
(Yes vs. no)	0.63	(0.40 – 0.98)	0.039
<b>Baseline Viral Load</b>			
(Per log <sup>10</sup> )	0.86	(0.73 – 1.00)	0.064

\* Behaviours refer to activities in the last six months.

\*\* Model was also adjusted for age, heroin injection and cocaine injection.