

Crystal methamphetamine and initiation of injection drug use among street-involved youth in a Canadian setting

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ABSTRACT

Background: Although injection drug use is known to result in a range of health-related harms, including transmission of HIV and fatal overdose, little is known about the possible role of synthetic drugs in injection initiation. We sought to determine the effect of crystal methamphetamine use on risk of injection initiation among street-involved youth in a Canadian setting.

Methods: We used Cox regression analyses to identify predictors of injection initiation among injection-naïve street-involved youth enrolled in the At-Risk Youth Study, a prospective cohort study of street-involved youth in Vancouver, British Columbia. Data on circumstances of first injection were also obtained.

Results: Between October 2005 and November 2010, a total of 395 drug injection-naïve, street-

involved youth provided 1434 observations, with 64 (16.2%) participants initiating injection drug use during the follow-up period, for a cumulative incidence of 21.7 (95% confidence interval [CI] 1.7–41.7) per 100 person-years. In multivariable analysis, recent noninjection use of crystal methamphetamine was positively associated with subsequent injection initiation (adjusted hazard ratio 1.93, 95% CI 1.31–2.85). The drug of first injection was most commonly reported as crystal methamphetamine (14/31 [45%]).

Interpretation: Noninjection use of crystal methamphetamine predicted subsequent injection initiation, and crystal methamphetamine was the most commonly used drug at the time of first injection. Evidence-based strategies to prevent transition to injection drug use among crystal methamphetamine users are urgently needed.

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Street-involved youth are at high risk of initiating injection drug use.¹ This situation is of concern, given that injection drug use has been associated with increased risk of transmission of HIV and hepatitis C virus^{2,3} and fatal overdose,⁴ as well as a range of other serious negative health and social outcomes. Newly initiated injection drug users have also been identified as a subpopulation at particularly high risk of injection-related harm.^{5–8} Unfortunately, despite recent calls to prioritize interventions to prevent the initiation of injection drug use,⁹ there are few evidence-based strategies to prevent injection initiation among street-involved youth.

This situation relates, in part, to the fact that little is known about the risk factors for injection initiation within this population. Prospective research from Montréal, Quebec, has alluded to the role that crack and powder cocaine may play in promoting subsequent injection initiation,¹⁰ as has retrospective research conducted among drug users in Baltimore, Maryland.¹¹ Much less is known about the possible role that synthetic drugs, such as methamphetamine, may play in contributing to an

increased risk of injection initiation.¹² Globally, amphetamine-type stimulants have emerged as one of the most commonly used groups of illicit drugs, second only to cannabis.¹³ This increase in amphetamine use is reflected in the epidemiology of drug use in some Canadian settings. For instance, in Vancouver, British Columbia, rates of injection use of crystal methamphetamine have increased significantly among adult injection drug users.¹⁴ This pattern is of substantial public health concern, given that crystal methamphetamine has been associated with a range of health and social harms, including the potential to drive high-risk drug-use patterns, including injection.¹⁵ Given these concerns and the well-established health-related harms of injection drug use, we investigated the possible role of crystal methamphetamine use in the incidence of first injection drug use within a cohort of street-involved youth in a Canadian setting.

Methods

The At-Risk Youth Study, established in 2005, is an open and ongoing prospective cohort study of street-involved youth aged 14 to 26 years based

in Vancouver.¹² All study participants were recruited through street outreach and self-referral. Consistent with previous studies of street-involved youth populations,^{10,16,17} potential participants were eligible if they had used illicit drugs other than marijuana in the past 30 days, if they provided written informed consent and if they were “street-involved.” Although there was no specific requirement that youth spend a minimum amount of time on the street to qualify for the study, in practice, the street-based recruitment produced a sample of youth who spent extensive time on the street, a large proportion of whom were homeless. Nevertheless, because our study lacked an explicit requirement that participants be living on the street, we use the term “street-involved youth,” rather than “street youth,” since the latter term is generally applied to youth known to live full-time or part-time on the street.¹⁸ Once enrolled, participants completed an interviewer-administered questionnaire (available by request to the corresponding author) at baseline, as well as physical and mental health assessments, including blood sampling for diagnostic testing and assessment for physical stigmata of injection drug use (i.e., track lines). Participants subsequently underwent physical examinations and completed interviewer-administered questionnaires semiannually; the questionnaires solicited basic sociodemographic and drug-use data, along with data on other relevant behaviours, including injection of drugs. Participants were given a \$20 honorarium at each visit. The study has been approved by the University of British Columbia/Providence Health Care Ethics Review Board.

The study presented here includes data collected from street-involved youth who were drug injection-naïve, who were enrolled in the At-Risk Youth Study cohort between Oct. 1, 2005, and Nov. 30, 2010, and who completed at least one follow-up interview. The outcome of interest was a first episode of any injection drug use. The primary independent variable of interest was any noninjection use of crystal methamphetamine (i.e., smoking and/or intranasal use) in the previous 6 months. Potential confounders identified in the literature and included in the study were age,¹⁰ sex (i.e., male v. female or male-to-female transgender), ethnicity (white v. other),^{19,20} recent (i.e., in the previous 6 months) noninjection heroin use,¹⁰ recent powder cocaine use (i.e., smoking and/or intranasal use),¹⁰ recent crack cocaine smoking,^{10,19,20} recent cannabis use^{19,20} and recent alcohol use.²⁰

First, we generated correlations between variables and tested for significant correlations using Pearson χ^2 tests. We used Kaplan–Meier methods to calculate the cumulative hazard of injection in-

itiation, stratified by crystal methamphetamine use. We then employed an a priori approach whereby basic sociodemographic variables (i.e., age, sex and ethnicity) were included in the final multivariable model, along with potential confounders significant at the $p < 0.05$ level in univariable testing. This approach reflects recent guidance from Rothman and Greenland²¹ encouraging specification of minimal models compatible with available information. Finally, we undertook a subanalysis investigating the circumstances of first injection in an effort to identify specific microsetting phenomena accompanying injection initiation events. All statistical analyses were performed using SPSS software version 17.0 (SPSS, Chicago, IL).

Results

A total of 991 participants completed the At-Risk Youth Study baseline questionnaire between October 2005 and November 2010, of whom 395 (39.9%) reported using crystal methamphetamine at baseline and 390 (39.4%) reported injecting drugs at baseline. Those with a history of injection drug use at baseline were more likely to use crystal methamphetamine than those without a history of injection drug use (183/390 [46.9%] v. 204/601 [33.9%], $p < 0.001$). Among the 601 individuals who were injection-naïve at baseline, 395 (65.7%) had a follow-up visit to assess for injection initiation and were therefore eligible for inclusion in the present study. The 206 injection-naïve participants who were ineligible for the present study because they had not yet returned for a follow-up

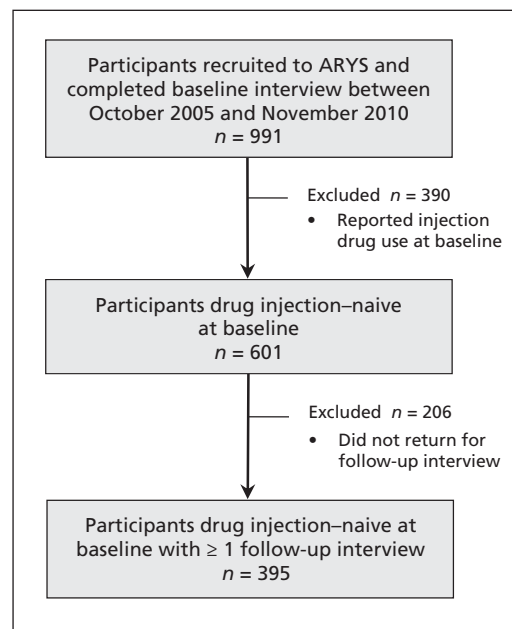


Figure 1: Flow diagram of recruitment and retention of participants in the At-Risk Youth Study (ARYS) and inclusion of participants in the current study.

interview did not differ significantly from the study sample in terms of sex (142/206 [68.9%] v. 269/395 [68.1%] male), ethnicity (140/206 [68.0%] v. 242/395 [61.3%] white) or baseline crystal methamphetamine use (67/206 [32.5%] v. 141/395 [35.7%]) (all $p > 0.05$), although there was a 1-year difference in median age (20.7 v. 21.6, $p = 0.002$). Figure 1 outlines the process of participant recruitment, retention and determination of eligibility for the present study.

In total, the 395 study participants provided 1434 observations over the study period. The median follow-up time was 21 (interquartile range [IQR] 13–26) months.

During the study period, 64 (16.2%) of the participants reported initiating injection drug use, for a cumulative incidence of 21.7 (95% confidence interval [CI] 1.7–41.7) per 100 person-years. The median age of first noninjection drug use was 14 (IQR 12–16) years among subsequent injection initiators and 12 (IQR 10–13) years among persistently injection-naïve participants. Among the 141 participants who reported noninjection use of crystal methamphetamine at baseline, 137 (97.2%) also reported cannabis use, 84 (59.6%) reported noninjection crack cocaine use, 67 (47.5%) reported noninjection powder cocaine use, and 32 (22.7%) reported noninjection heroin use (Table 1).

Ethnicity was highly and significantly correlated with all other variables, including crystal methamphetamine use (Pearson $r = 0.755$, $p < 0.001$) (Table 2). After 36 months, the cumulative hazard of injection initiation was higher among participants who reported crystal methamphetamine use

than among those who did not report use of this drug (32.3% v. 13.3%; $p = 0.010$) (Figure 2).

In the multivariable analysis, recent noninjection crystal methamphetamine use (adjusted hazard ratio [HR] 1.93, 95% CI 1.31–2.85) and recent noninjection heroin use (adjusted HR 1.73, 95% CI 1.09–2.74) were associated with an increased risk of injection initiation (Table 3). By contrast, older age (adjusted HR 0.81, 95% CI 0.75–0.88) and white ethnicity (adjusted HR 0.24, 95% CI 0.11–0.49) were negatively associated with the risk of injection initiation.

Among participants who responded to questions on the circumstances of their initiation events, 50% (15/30) reported receiving their first injected drug as a gift. The drug of first injection was most commonly crystal methamphetamine (14/31 [45%]), followed by heroin (9/31 [29%]) and cocaine (3/31 [10%]). Almost all respondents (16/17 [94%]) reported that they did not believe that their use of drugs was out of control before the first injection. Furthermore, 19 (68%) of 28 participants reported that they had not considered injecting before the initiation event.

Although the reported microsettings for injection initiation were diverse, 12 (39%) of 31 participants reported initiating injection drug use in an outdoor public space. In terms of geographic setting, the largest proportion of participants reported initiating injection in Vancouver's Downtown Eastside neighbourhood (14/30 [47%]), the site of a large open-air illicit drug market. Another 20% (6/30) reported initiating injection in the Downtown South, an adjacent neighbourhood previously identified as a poten-

Table 1: Baseline characteristics of drug injection-naïve, street-involved youth according to noninjection use of crystal methamphetamine, Vancouver, British Columbia

Characteristic	Use of crystal methamphetamine; no. (%) of participants*		
	Total <i>n</i> = 395	No <i>n</i> = 254	Yes <i>n</i> = 141
Sociodemographic			
Age, yr, median (IQR)	21.6 (19.6–23.3)	21.7 (19.5–23.6)	21.4 (19.7–22.8)
Sex, male	269 (68.1)	177 (69.7)	92 (65.2)
Ethnicity, white	242 (61.3)	147 (57.9)	95 (67.4)
Recent drug use†			
Cocaine	194 (49.1)	127 (50.0)	67 (47.5)
Crack cocaine	221 (55.9)	137 (53.9)	84 (59.6)
Heroin	63 (15.9)	31 (12.2)	32 (22.7)
Cannabis	389 (98.5)	252 (99.2)	137 (97.2)
Alcohol	69 (17.5)	50 (19.7)	19 (13.5)

Note: IQR = interquartile range.
 *Except where indicated otherwise.
 †All drug-use variables refer to noninjection use in the preceding 6 months.

tial geographic area of transition into drug dependence among street-involved youth.²²⁻²⁴ Participants reported that a variety of individuals were present at initiation events, including friends (17/30 [57%]), family members (4/30 [13%]) and acquaintances (3/30 [10%]). However, 17% of respondents (5/30) reported initiating injection drug use alone. All but one of the initiates (30/31 [97%]) reported that they had not shared needles during their first injection experiences. A majority of participants (25/31 [81%]) reported that someone else performed the injection during the initiation event. Finally, fewer than half of participants (12/29 [41%]) reported subsequently becoming regular injection drug users during the study period.

Interpretation

Within a sample of street-involved youth in a Canadian setting, recent noninjection use of crystal methamphetamine was independently associated with an increased risk of subsequent initiation of injection drug use. Furthermore, within a subsample of first-time injection drug users, crystal methamphetamine was most commonly reported as the drug used during initiation events. Most studies of injection initiation have employed cross-sectional or retrospective data.^{11,20,25-27} The retention rate of the current longitudinal study (65.7%) was comparable to that of other longitudinal studies of injection initiation (64%,²⁸ 67%²⁹) but somewhat lower than that reported in another Canadian study

Table 2: Correlations between independent variables of interest

Variable	Ethnicity, white	Sex, male	Age, yr	Recent drug use					
				Cocaine	Crack	Heroin	Crystal methamphetamine	Cannabis	Alcohol
Ethnicity, white									
Pearson correlation	1	0.004	-0.185	0.717	0.676	0.838	0.755	0.804	0.790
<i>p</i> value (2-tailed)	NA	0.888	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Sex, male									
Pearson correlation		1	0.218	0.017	0.029	-0.018	-0.015	0.121	0.011
<i>p</i> value (2-tailed)		NA	< 0.001	0.559	0.310	0.532	0.606	< 0.001	0.714
Age, yr									
Pearson correlation			1	-0.198	0.056	-0.110	-0.093	-0.152	-0.158
<i>p</i> value (2-tailed)			NA	< 0.001	0.052	< 0.001	0.001	< 0.001	< 0.001
Recent drug use*									
<i>Cocaine</i>									
Pearson correlation				1	0.528	0.627	0.555	0.639	0.644
<i>p</i> value (2-tailed)				NA	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
<i>Crack</i>									
Pearson correlation					1	0.666†	0.546	0.589	0.556
<i>p</i> value (2-tailed)					NA	< 0.001	< 0.001	< 0.001	< 0.001
<i>Heroin</i>									
Pearson correlation						1	0.689	0.666	0.661
<i>p</i> value (2-tailed)						NA	< 0.001	< 0.001	< 0.001
<i>Crystal methamphetamine</i>									
Pearson correlation							1	0.642	0.572
<i>p</i> value (2-tailed)							NA	< 0.001	< 0.001
<i>Cannabis</i>									
Pearson correlation								1	0.658
<i>p</i> value (2-tailed)								NA	< 0.001
<i>Alcohol</i>									
Pearson correlation									1
<i>p</i> value (2-tailed)									NA

Note: NA = not applicable.

*All drug-use variables refer to noninjection use in the preceding 6 months.

of injection initiation (in Montréal), which had a follow-up rate of 89%.¹⁰

Canadian surveillance data suggest that reported levels of crystal methamphetamine use in the previous 3 months among street-involved youth aged 15–24 years increased significantly in the early 2000s, from 2.5% in 1999 to 9.5% in 2005.³⁰ This trend is consistent with global patterns of crystal methamphetamine use, according to data from the United Nations Office on Drugs and Crime.¹³ Indeed, methamphetamine remains widely available, and levels of methamphetamine use remain high among youth, particularly in Southeast Asia and North America.¹³ This likely reflects the relative ease with which amphetamine-type stimulants can be produced, as well as the fact that, unlike available opioid-substitution treatments, few effective stimulant-substitution treatment options exist.³¹ Furthermore, a recent review of clinical treatment for methamphetamine dependence noted the dearth of effective treatment options for this drug, stating that one barrier to the development of treatment has been inadequate research on the characteristics and consequences of use of this drug.³¹

The data presented here appear highly relevant in the context of these upward trends. Specifically, whereas previous research has identified a variety of serious health harms associated with crystal methamphetamine use,³² the current study has identified use of this drug as a risk factor for injection

initiation. Although the data were incomplete, we found in the present study that not only was non-injection use of crystal methamphetamine associated with subsequent injection drug use, but also that crystal methamphetamine was most commonly reported as the drug of first injection. These results differ from a study of street youth in Montréal, in which use of cocaine (both powder and crack cocaine) was significantly associated with subsequent injection initiation. However, rates of methamphetamine use were much lower in that setting. Notably, although both crack cocaine and methamphetamine are commonly used and widely available,¹⁴ the independent effect of methamphetamine on increasing the risk of injection initiation in the current study nevertheless remained.

With respect to specific drug-related risks for initiation, both the Risk Evaluation and Assessment of Community Health (REACH) III study²⁰ and the Montréal Street Youth Cohort study¹⁰ concluded that individuals identified as being at high risk of initiating injection drug use require more peer-delivered information regarding different routes of drug administration (e.g., injection v. noninjection) and their consequences. To that end, some studies have suggested that older injection drug users should be enlisted in efforts to educate younger drug users regarding the harms of transitioning to injection drug use.³³ Our current findings regarding the microsetting characteristics of injection initiation events elucidate the context-

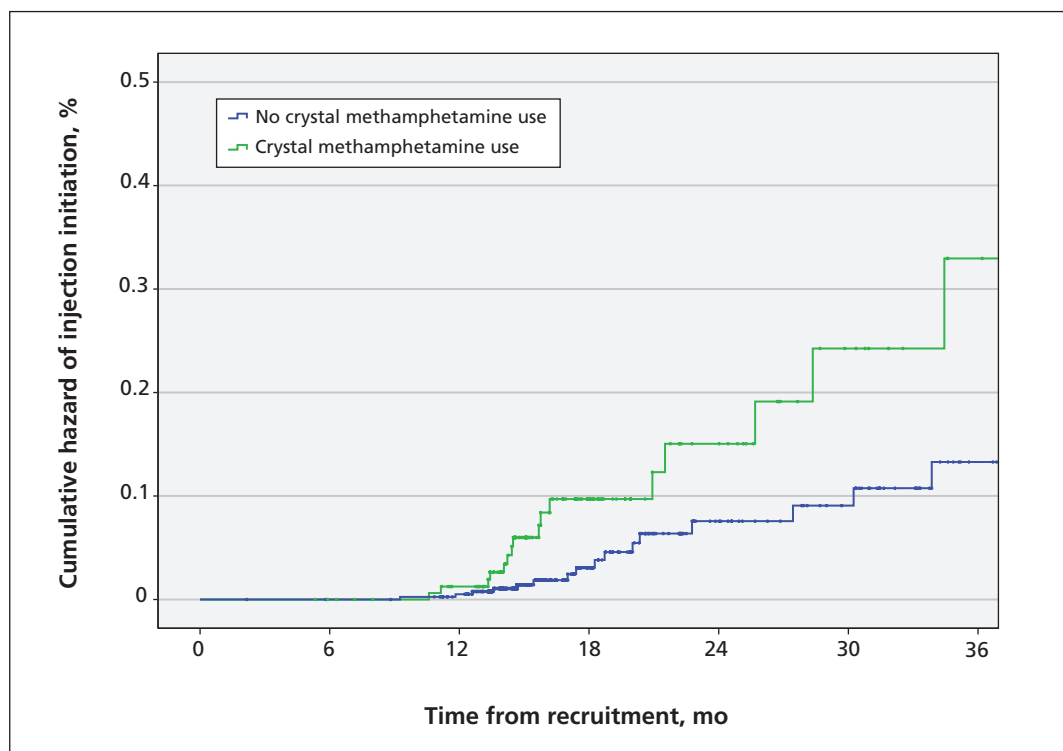


Figure 2: Cumulative hazard of injection initiation among street-involved youth, stratified by use of crystal methamphetamine in Vancouver, British Columbia, October 2005 to November 2010 ($n = 395$).

specific roles that other injection drug users may play in determining risk of injection initiation among street-involved youth. Specifically, half of the subsample of injection initiators reported receiving the injected drug as a gift, and over four-fifths reported that someone else had performed the injection during their initiation event. These findings suggest that drug-using peers and established injection drug users may play a critical role in initiating street-based young people into injection drug use through a variety of roles. However, one potential avenue to mitigate the impact of established injection drug users may be increasing community access to evidence-based forms of addiction treatment. Given that this approach has the potential to reduce the overall number of injection drug users in a community, it may therefore help in reducing youth exposure to established injection drug users in general.

Limitations

This study had limitations consistent with observational studies of drug-using populations. First, although the At-Risk Youth Study reflects many characteristics representative of street-involved youth living in Vancouver,^{34,35} the lack of registries of such young people meant that recruitment was not randomized. The generalizability of this study may therefore be limited, particularly as few, if any, previous studies have been able to investigate the potential role of crystal methamphetamine use in increasing the risk of injection initiation among street-involved youth. Second, the potential exists that those injection-naïve participants who were

lost to follow-up may have differed from the study participants on other unmeasured factors that could have affected the study findings. In this regard, it is noteworthy that those lost to follow-up did not differ significantly in terms of crystal methamphetamine use or key sociodemographic factors other than age. Third, illicit drug use remains highly stigmatized, which may have affected participants' responses,³⁶ although such bias might not have affected the response patterns of initiators and non-initiators differently. Fourth, we cannot rule out the potential for confounding as a result of exposures or participant traits that were not measured as part of the present study. For instance, illicit stimulant use has been associated with psychiatric disorders, including attention-deficit/hyperactivity disorder.^{37,38} Unfortunately, standardized assessment of psychiatric disorders was not undertaken as part of the At-Risk Youth Study. Similarly, there is increasing recognition of genetic factors that may predispose individuals to addictive disorders and high-risk drug use,³⁹ and these data were also not available in the present study. Nevertheless, we identified a strong independent association between crystal methamphetamine use and subsequent injection drug use, a finding with immediate policy implications. Finally, data on the circumstances of injection were not available for all incident cases of injection initiation. Further research, including qualitative methods, may be useful in more fully elucidating the lived experience of drug-use activities and the social circumstances that contribute to initiation of injection drug use in high-risk populations.

Conclusion

In this study of drug-related risks for injection initiation among street-involved youth, noninjection use of crystal methamphetamine was independently associated with an increased risk of injection initiation, after adjustment for socio-demographic and drug-related confounders. In a subanalysis of the circumstances of first injection, the largest proportion of participants reported initiating injection with crystal methamphetamine. Addressing the impact of crystal methamphetamine use in increasing the risk of injection initiation among injection-naïve street-involved youth represents an urgent public health priority.^{9,40} Development and evaluation of appropriate interventions are therefore critically needed. Indeed, consistent with calls for an increased focus on the prevention of injection drug use,^{9,40} further research is required to develop and test evidence-based interventions to prevent injection drug use in ways that accommodate the complexities of crystal methamphetamine and polydrug use.

Table 3: Unadjusted and adjusted hazard ratios for factors related to initiation of injection drug use among street-involved youth in Vancouver, British Columbia, 2005–2010 (*n* = 395)

Characteristic	Hazard ratio (95% CI)	
	Unadjusted	Adjusted
Sociodemographic		
Age (per yr older)	0.91 (0.86–0.97)	0.81 (0.75–0.88)
Male sex	0.61 (0.42–0.88)	0.90 (0.60–1.36)
White ethnicity (v. other)	1.28 (0.87–1.89)	0.24 (0.11–0.49)
Recent drug use*		
Cocaine	0.94 (0.73–1.21)	—
Crack	1.20 (0.93–1.56)	—
Heroin	1.39 (1.06–1.82)	1.73 (1.09–2.74)
Crystal methamphetamine	1.51 (1.19–1.99)	1.93 (1.31–2.85)
Cannabis	0.94 (0.67–1.26)	—
Alcohol	1.02 (0.77–1.37)	—

Note: CI = confidence interval.
*All drug-use variables refer to noninjection use in the preceding 6 months.

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