

IMPLICATIONS AND CONTRIBUTION

Patterns of injection drug use cessation remain poorly described. Among a prospective cohort of street-involved youth, nearly half ceased injecting for ≥ 6 months during the 10-year study period. Youth injecting heroin or crystal methamphetamine were less likely to cease injecting, and cessation was frequently accompanied by ongoing non-injection drug use.

ABSTRACT

Purpose: Injection drug use is prevalent among street-involved youth, but patterns of cessation are poorly described. We identified drug use patterns preceding injection cessation among street-involved youth.

Methods: From September 2005 to May 2015, we collected data from the At-Risk Youth Study, a prospective cohort of street-involved youth in Vancouver, Canada, and limited the sample to actively injecting youth. The primary outcome was cessation of injecting self-reported at semiannual follow-up visits. We used Cox regression to identify drug use patterns preceding cessation.

Results: Among 383 youth, 65% were male, mean age was 22.3 (SD, 2.5; range, 15-30) years, and 171 (45%) ceased injecting for 6 months or more (crude incidence density 22 per 100 person-years; 95% confidence interval [CI], 19-26). Youth who ceased were less likely to have injected daily (adjusted hazard ratio [AHR], 0.40; 95% CI, 0.28-0.56), injected heroin (AHR, 0.40; 95% CI, 0.29-0.56), or injected crystal methamphetamine (AHR, 0.43; 95% CI, 0.31-0.59) prior to cessation. Non-injection heroin use was positively associated with injection cessation (AHR, 1.52; 95 CI, 1.12-2.08). Addiction treatment was not associated with cessation. At the time of cessation, 101 (59%) youth continued to use 'hard' non-injection drugs such as heroin and crystal methamphetamine.

Conclusions: Periods of injection cessation were common but frequently accompanied by ongoing non-injection drug use. Findings indicate that trajectories of injection drug use among youth are complex and highlight the need to further explore relationships between ongoing non-injection drug use and injection cessation.

INTRODUCTION

Street youth – that is, young people who live or work on the street – are a marginalized population with excess morbidity and mortality relative to the general population of adolescents and young adults [1,2]. Injection drug use is prevalent among street youth [1,3], and is associated with risk for death, as well as non-fatal overdose and infection with human immunodeficiency virus (HIV) and hepatitis C virus [2,4–7]. Although data suggest that once they initiate injecting youth are at risk of rapidly transitioning to regular use, less is known about transitions out of injection [8]. Some youth who inject may cease injection, either by exclusively using non-injection drugs or by abstaining from drug use altogether [9]. Patterns of drug use preceding and accompanying injection cessation among youth remain poorly described, thus hampering clinicians, researchers, and policymakers from directing interventions to support cessation.

The majority of studies to date examining injection cessation have focused on older populations of people who inject drugs [10–13]. In these studies, those who were least likely to cease injection were those who were younger at age of first drug use [10–13], injected daily [10], or injected heroin or cocaine [10,12]. Since intervening early in the trajectory of injection drug use may help avert lifelong harms associated with addiction, it is critical to identify drug use patterns that may precede or accompany (and thus facilitate or impede) cessation among young people. Furthermore, conducting studies of youth in the community may help better elucidate the natural history of injection drug use, as compared to studies in treatment settings where individuals may offer socially desirable reporting in the presence of clinicians actively managing their addiction care [14]. Recent data from street youth recruited from community settings are needed, particularly in light of the emerging understanding of risk associated with crystal methamphetamine injection amidst an ongoing heroin and prescription opioid crisis [15–18].

Drawing on a prospective cohort study of street-involved youth in a Canadian setting with

high prevalence of injection drug use, we undertook the present study to characterize the prevalence of injection cessation and identify the patterns of drug use that precede cessation events. We also sought to determine whether abstinence from all substances was common after cessation, or whether ongoing non-injection drug use was more frequently observed.

METHODS

Participants

The At-Risk Youth Study (ARYS) is a prospective cohort study of street youth based in Vancouver, Canada. The study has been described previously [3]. In brief, from September 2005 to May 2015, youth of age 14-26 years who had used any illicit drug (other than or in addition to marijuana) in the preceding 30 days were eligible for study enrollment. Recruited youth were street-involved, defined as have been absolutely or temporarily without stable housing or having accessed street-based services in the preceding six months [1,6]. Street-based outreach was used to enhance study recruitment in Vancouver neighborhoods where street youth are known to congregate, and snowball sampling was used to maximize enrollment.

After providing informed consent, participants completed an interviewer-administered questionnaire regarding sociodemographic details and both non-injection and injection drug use patterns. Participants then returned at six-month intervals thereafter for follow-up visits to reassess their drug use behaviors. All participants were provided \$30 CAN at baseline and for each completed follow-up visit as remuneration for their time. ARYS was approved by the University of British Columbia and Providence Health Care Research Ethics Board.

The present analysis was restricted to participants who reported active injection (*i.e.*, those who reported any drug injection during the preceding six months, either at their baseline visit or

at any follow-up visit) and who returned for at least one subsequent follow-up visit after they first reported injecting to assess for cessation. Depending on the visit at which they first reported injecting, youth could be older than the maximum enrollment age of 26 years at the time they entered into the analytic sample.

Outcomes and exposures

The primary outcome of interest was self-reported cessation of injection drug use during the preceding six months reported at any follow-up visit. Specifically, participants were asked, “In the last six months, have you used a needle to chip, fix, or muscle even once (Yes/No)?”

We then examined drug use patterns potentially associated with the time to cessation of injection drug use. To determine self-reported drug use patterns that preceded injection cessation, measures were taken from the study follow-up visit that preceded the visit at which a participant reported cessation of injection, and examined the reported drug use patterns at that preceding visit. Covariates included separate questions regarding injection and non-injection drug use patterns (all coded “any/none”) with regard to: daily drug use, heroin use, prescription opioid use (including dilaudid, morphine, codeine, street methadone, oxycodone, and pentazocine), crystal methamphetamine use, cocaine use, and crack use. Covariates also included polysubstance injection (injection of any 2 or more of [*i*] heroin/prescription opioids, [*ii*] crystal methamphetamine, or [*iii*] cocaine/crack), and engagement in addiction treatment (including methadone maintenance, outpatient treatment, residential treatment, Narcotics’ Anonymous, or detoxification).

We also examined age of first drug use as a potential covariate (as a continuous variable), as well as sociodemographic factors including age (as a continuous variable), self-identified gender, Indigenous ancestry (“First Nations”, “Aboriginal”, “Inuit”, “Métis”, or any other identification with a recognized indigenous group), prior completion of or current enrollment in high school, homelessness in the preceding six months, incarceration in the preceding six

months, any hospitalization in the preceding six months, and self-reported lifetime history of mental illness. Variables were selected *a priori* based on the prior literature [9–12].

Analyses

We compared sociodemographic characteristics and drug use behaviors between those who did and did not cease injection drug use at any time during follow-up using Pearson χ^2 test and Fisher's exact test (for cell counts under 5) for categorical variables and the Wilcoxon test for continuous variables. Then, using the Kaplan-Meier method, we compared the cumulative incidence of cessation according to past-6-month injection use (as reported at the follow-up visit immediately preceding a visit at which a participant reported cessation) of five substances: heroin, prescription opioids, crystal methamphetamine, cocaine, and crack. Participants were right-censored at the time of their first cessation event (*i.e.*, no further person-time at risk was contributed by that participant), but if they reported resuming injection drug use at a later visit, they reentered the cohort of individuals at risk; participants who did not report any cessation were right-censored at the time of their last follow-up visit. We then compared survival distributions using the log-rank test.

Using an extended Cox model with time-dependent variables, we then examined bivariate associations between each of the sociodemographic and drug use variables and time to injection cessation. Variables significant at $p < 0.10$ in bivariate analyses were eligible for inclusion in the multivariate model, which used backward selection to identify the model of best fit based on minimizing the Akaike information criterion (AIC). Finally, we quantified ongoing non-injection drug use during the 6-month period that youth reported having ceased injection. Analyses were performed using RStudio Version 0.99.892 (RStudio, Boston, MA).

RESULTS

Of 383 actively drug-injecting youth who were eligible for inclusion in the analysis, 248 (65%) were male and 85 (22%) identified as being of Indigenous ancestry. Mean age was 22.3 (SD, 2.5) years at baseline. An additional 151 youth reported injection drug use at study enrollment but did not return or were not yet eligible for inclusion given the open prospective nature of the cohort. The 383 youth who completed a study follow-up visit were similar to the 151 who did not with regard to all study variables at baseline ($p > 0.05$ for all), with the exception that individuals who did not complete a study follow-up visit were more likely to have begun using drugs at a younger age ($p = 0.029$) and inject cocaine ($p = 0.008$).

Participants in the study sample contributed 765 person-years of total follow-up with a median of 19 months (interquartile range [IQR], 10-31; range, 5-111) of follow-up per participant. Cessation of injection drug use during follow-up was reported by 171 (45%) youth, resulting in a crude incidence density of 22 per 100 person-years (95% confidence interval [CI], 19-26 per 100 person-years). The median time from the first report of injection drug use during the study period to the first report of injection cessation was 13 months (IQR, 7-24; range, 5-97). Among the 171 youth who ceased injection during study follow-up, 120 (70%) returned for a subsequent study visit to assess for relapse into injecting. Sixty-six of these youth (55%) reported reinitiating injecting at a later follow-up visit. The median number of months of follow-up post injection cessation among the 120 youth who returned for at least one study visit was 22 (IQR, 12-44; range, 4-102).

Table 1 shows sociodemographic characteristics and drug use behaviors at baseline, comparing those who did and did not cease injecting during follow-up. Youth did not differ based on sociodemographic factors, but at baseline, those who ceased were significantly less likely to report daily injection drug use; injection of heroin, prescription opioids, and crystal

methamphetamine; and polysubstance injection use. Youth who ceased were not more likely to have received addiction treatment.

As shown in **Figure 1A-F**, the cumulative incidence of cessation was significantly lower among those who reported recent injection of heroin, prescription opioids, crystal methamphetamine, and crack, but not among those who reported recent injection of cocaine. Heroin was the most commonly used substance prior to cessation (92 youth, 54%), followed by crystal methamphetamine (85 youth, 50%), cocaine (40 youth, 23%), prescription opioids (37 youth, 22%), and crack (6 youth, 4%).

Table 2 lists unadjusted and adjusted hazard ratios (HR) for cessation of injecting and variables of interest including sociodemographic and drug use variables. Adjusted models demonstrated that cessation was significantly less likely among those who had recently experienced homelessness or incarceration, or who at the visit prior to cessation had engaged in daily injecting or injection of heroin or crystal methamphetamine. Conversely, cessation was significantly more likely among those who were using heroin via non-injection routes at the visit prior to cessation. Receipt of addiction treatment was not associated with cessation.

At the time of their reported cessation event, 40 (23%) youth had ceased all non-injection drug use as well. An additional 30 (18%) youth used only marijuana, having ceased all other non-injection drugs. Of the remaining 101 youth who used non-injection drugs (other than marijuana), 36 (36%) reported using non-injection drugs on a daily basis. The most common non-injection drugs that these 101 youth reported using at the time of cessation included crystal methamphetamine (56 youth, 55%), crack (51 youth, 50%), cocaine (32 youth, 32%), heroin (22 youth, 22%), ecstasy (15 youth, 15%), benzodiazepines or other sedatives (13 youth, 13%), and prescription opioids (9 youth, 9%); 57 (56%) youth used two or more non-injection drugs at the time of cessation. Among these 101 youth, 69 (68%) also reported marijuana use at the time of

injection cessation.

DISCUSSION

In this prospective cohort of actively injecting street youth, we observed that more than 4 in 10 youth ceased injection for at least 6 months. Youth who ceased were less likely to have recently experienced homelessness or incarceration, or at the visit prior to cessation, engaged in daily injecting or injection of heroin or crystal methamphetamine, and were more likely to be using heroin via non-injection routes of administration. More than one-third of youth who ceased injecting were observed to relapse into injection (39%); furthermore, the majority of youth who ceased injection continued to use “hard” drugs via non-injection routes (59%), and an additional 18% continued to use marijuana.

Our findings build on two prior studies of cessation among street youth conducted in Montreal between 1995-2000 [9] and in San Francisco between 2000-2008 [19]. These studies reaffirmed that younger age of first drug use and more frequent injecting were associated with reduced likelihood of cessation [9,19]. Although these studies found that youth who injected cocaine were less likely to stop injecting, our findings suggest that amidst the highly prevalent use of heroin and crystal methamphetamine, use of these substances appears to also substantially impede cessation. Both heroin and crystal methamphetamine are also strongly linked to increased risk for HIV and hepatitis C virus transmission among people who inject drugs [16,18,20–23]. Notably, unlike these prior studies, we did not find a significantly different age of first drug use between youth who ceased and those who did not. Our findings thus underscore the need for interventions that not only reduce injection-related harm, but also provide additional support for individuals who may wish to stop injecting methamphetamine or opioids but may be having difficulty doing so. Given that recently homeless and incarcerated youth were less likely to cease

injection drug use, critical supports might include stable housing and approaches to support justice system-involved youth [24].

The finding that youth using heroin were less likely to cease injecting, coupled with the lack of an association of addiction treatment with cessation, suggests that current addiction treatment services may not meet the needs of vulnerable youth [25,26]. It is noteworthy that the majority of cessation events coincided with continued non-injection drug use. Therefore, while addiction treatment engagement may support abstinence from substance use, our findings suggest that it may not be optimally supporting transitions to lower-risk substance use patterns with significant risk reduction. Future studies should identify contextual and drug use-related factors that influence the timing of intervals of cessation and relapse, including the influence of peers/partners, and medical comorbidity (such as infection with HIV or hepatitis C), psychiatric comorbidity, and access to and cost of drugs.

Historically, in many treatment settings, young people with opioid use disorder have not been offered medication-assisted treatment (including pharmacotherapy with methadone, buprenorphine, or naltrexone) [27], which have been shown to reduce opioid withdrawal, improve avoidance of opioids, and reduce the frequency of injection drug use [28,29]. Providers may not have experience offering medication-assisted treatment to young people, or may be less likely to prescribe medications when encountering a young person, whose history of injecting is likely to be shorter than that of older individuals [30]. A recent policy statement supports use of medication-assisted treatment for youth with opioid use disorder [31], and as this practice becomes increasingly common, future studies should examine the extent to which medications promote and sustain cessation of injecting.

Interventions that take into account the unique psychosocial and developmental needs of street youth are needed [32,33]. Prior studies have shown that youth who use drugs (and in particular, youth of indigenous ancestry) experience multiple barriers to completing treatment,

including long wait lists, difficulty with program rules or expectations, and in other settings where universal health care is not available, inability to pay or rejection of treatment coverage by insurance companies [34,35]. Our findings also demonstrate that innovative approaches to stimulant use disorder are needed. Since treatment of opioid use disorder has benefitted greatly from the availability of agonist medications, treatment of methamphetamine use disorder similarly might benefit from availability of pharmacotherapy options. Regardless, the finding that addiction treatment was not associated with cessation of injecting deserves further study to elucidate ways in which current treatment paradigms may not meet the needs of vulnerable youth. Indeed, there is a dearth of youth-specific interventions to promote cessation of injecting and this should remain an area of development.

Our results also highlighted that youth who stopped injecting were more than 50% more likely than those who did not have used non-injection heroin. For some street youth, injection drug use is a dynamic process marked by transitions into and out of injecting [9]; thus, it is possible that some youth were using heroin via non-injection routes during the natural course of their drug use, and that use of heroin via non-injection routes was a marker for lower dependence on injecting as a route of administration. However, in light of clinical trials demonstrating that non-injectable heroin can be used to promote cessation of injecting heroin and other drugs [36,37], it is also possible that some youth may have been using heroin via non-injection routes as a means of actively weaning themselves from injection drug use. This finding supports harm reduction efforts that seek to reduce the adverse consequences of injection drug use by supporting youth who may not be prepared to abstain from substances altogether.

Similarly, since many youth smoked marijuana during the same six-month window as their cessation event, it is possible some youth may have been using marijuana to manage cravings and withdrawal symptoms following injection cessation [38,39]. Future exploration of these associations is warranted, including closer examination of how other non-injection drug use may

influence transitions into and out of injection drug use, as well as whether continued non-injection drug use is associated with an elevated risk of relapse into injecting. In particular, qualitative or mixed methods approaches would be well suited to describe these transitions.

There are limitations to this study. First, because street youth are a marginalized group that typically evades standard population-based sampling methods, we used snowball sampling. This approach does not provide a truly random sample, although it is noteworthy that the characteristics of the ARYS sample is similar to those from other studies of high-risk youth [9,19]. Second, our findings are limited to youth who provided follow-up data after their baseline visit. We noted that youth with earlier onset of drug use and recent cocaine injection were less likely to return for follow-up, and prior studies of street youth elsewhere suggest that these same youth may be less likely to cease injection drug use [9]. Third, we relied on self-report, which may have been subject to socially desirability bias. Despite assurances of confidentiality, we cannot exclude that some participants may have been reluctant to disclose some behaviors, which may have affected our primary outcome, cessation of injecting, if youth felt uncomfortable revealing that they were still injecting at the time of the interview. Nonetheless, a large number of youth felt comfortable disclosing their ongoing substance use and injecting behaviors.

Street youth who inject are at greatly elevated risk of early death and infectious disease transmission [1,2]. However, given their young age, there may be unique opportunities to intervene early and mitigate a life course trajectory towards long-standing substance use and injection-related harm. Acknowledging that injecting certain drugs – namely heroin and crystal methamphetamine – may make youth less likely to cease injecting, evidence-based treatment services that specifically address use of these substances may help promote sustained cessation. Given the prevalence of sustained non-injection substance use after cessation, further research on the relationship between non-injection drug use patterns and injecting trajectories is necessary and would inform addiction treatment.

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FIGURE 1A-F: Cumulative incidence of ceasing injection drug use according to whether during the preceding 6 months participant had injected (A) heroin, (B) prescription opioids, (C) crystal methamphetamine, (D) cocaine, (E) crack, or (F) two or more substances: At Risk Youth Study (ARYS), Vancouver, British Columbia, 2005-2015 ($n = 383$).