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PATTERNS OF NON-INJECTION DRUG USE ASSOCIATED WITH INJECTION CESSATION AMONG STREET-INVOLVED YOUTH IN VANCOUVER, CANADA

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ABSTRACT

Although abstinence from drug use is often a key goal of youth substance use treatment, transitioning to less harmful routes and types of drug use is desirable from both a clinical and public health perspective. Despite this, little is known about the trajectories of youth who inject drugs including changes in patterns of non-injection drug use. The At-Risk Youth Study (ARYS) is a longitudinal cohort of street-involved youth who use drugs in Vancouver, Canada. We used linear growth curve modeling to compare changes in non-injection drug use among participants who ceased injecting drugs for at least one six-month period between September 2005 and May 2015 to matched controls who continued injecting over the same period. Of 387 eligible participants, 173 (44.7%) reported ceasing drug injection at least once. Non-injection drug use occurred during 160 (79.6%) periods of injection cessation. In adjusted linear growth curve analyses, the only non-injection drug use pattern observed to decrease significantly more than controls following injection cessation was daily crack/cocaine use (p = 0.024). With the exception of frequent crack/cocaine use, transitions out of injection drug use did not appear to coincide with increased reductions in patterns of non-injection drug use. Our findings indicate that most (80%) of the observed injection cessation events occurred in the context of ongoing substance use. Given that transitioning out of drug injection represents a significant reduction in risk and harm, efforts supporting vulnerable youth to move away from injecting may benefit from approaches that allow for ongoing non-injection drug use.

Word Count: 250

Keywords: Injection drug use, Injection cessation, Crack, Cocaine, Youth

INTRODUCTION

Reducing the burden of disease attributable to substance use among young people is a growing public health priority globally.[1] Among street-involved youth (i.e., young people who live and/or work on the street),[2,3], injection drug use is a central public health concern, as it increases susceptibility to a range of severe drug-related morbidity and mortality including HIV[4,5] and hepatitis C infection,[6,7] bacterial infections (e.g., endocarditis),[8] and overdose.[9,10] In settings across Canada, almost half of street-involved youth report a history of injection drug use,[11,12] and the majority of youth who initiate injecting drugs will progress to regular injection use within one month of their first injection.[13] Street-involved youth experience a mortality rate approximately 11 times higher than that of the age- and sex-matched general population[2,3,14] due to overdose, suicide, trauma/accidents, and medical conditions related to injection drug use.[15] Not surprisingly, injection drug use is a major predictor of mortality among them.[2]

It has long been recognized that injecting careers are dynamic and complex processes, often involving recurring cessation and relapse,[16] yet much of the research into injection trajectories among at-risk youth has focused on risk factors for injection initiation,[17-20] while transitions out of injection drug use have not been as well characterized. Although many young individuals struggling with substance use disorders have benefitted from abstinence-based treatment models, it is also becoming increasingly clear, from high drop out and relapse rates,[21-24] that they are far from universally beneficial and may even set the stage for severe drug-related harms. For example, the many individuals who relapse after discharge from abstinence-oriented treatment programs are highly susceptible to fatal overdose as a result of reduced drug

tolerance.[25-28] In many settings, there is a significant portion of youth who do not access substance use treatment for various reasons including choosing to "handle their drug problem on their own".[29] From a public health perspective, for those unable or unwilling to cease drug use completely (engaged in treatment or not), reducing use, transitioning from injection drug use to lower-risk methods of drug administration (e.g., smoking, intranasal) and/or comparatively less harmful drugs (e.g., cannabis) is considered favourable to continued injection drug use.[30,31] This consideration is increasingly being adopted among substance use care experts as a valid option on the substance use care spectrum that can contribute to improved health on its own [32] or as part of a long-term bridge to abstinence.[33,34] Ongoing non-injection drug use has been previously documented among youth throughout periods of injection cessation; for example, in a study of young people who inject drugs in Montreal, Canada, approximately one-third of those who ceased injecting drugs did not abstain from heroin and cocaine use during cessation.[35] However, very little is known about how patterns of non-injection drug use may change during transitions out of injection drug use. For example, the extent to which injection cessation is accompanied by transitions to complete abstinence from other forms of drug use, reductions in other modes of use, or even increases in other modes of use (i.e., substitution), has received little consideration in the context of public health approaches to harm reduction and drug treatment for youth.

Therefore, we conducted the present study among youth and young adults who inject drugs in Vancouver, Canada to: (1) examine how non-injection drug use changes from periods of active injection to periods of cessation of injection, and (2) determine how these changes may differ from youth and young adults who continue to engage in active injection drug use.

METHODS

Study Sample

Data for this study was derived from the At-Risk Youth Study, an ongoing prospective cohort of vulnerable street-involved youth and young adults who use illicit drugs. This study has been described in detail previously.[36] In brief, participants are recruited through self-referral, snowball sampling, and extensive street outreach in various areas of downtown Vancouver including the Downtown Eastside (DTES), a lower-income neighbourhood known for its open illicit drug use scene, and the Downtown South, an area often frequented by transient, homeless, or vulnerable youth. To be eligible for ARYS, participants must provide written informed consent, be under 26 years of age, report using an illicit drug other than (or in addition to) cannabis in the month prior to enrolment, and self-identify as "street involved," defined as being recently homeless or having used services designated for street-involved youth in the preceding six months.[2,37]

At baseline and bi-annually, participants complete an interviewer-administered questionnaire eliciting information on time-updated socio-demographic, behavioural, and health-related exposures. Each participant also undergoes a consultation with a study nurse, and is referred to appropriate health care services if needed. All participants receive a $30 (CAD) honorarium upon completion of each study visit. The University of British Columbia/Providence Health Care Research Ethics Board provided ethical approval for this study.

Measures

As we were interested in examining cessation of injection drug use, we restricted the study sample to youth who reported injection drug use at their baseline interview or at any point during the study period. Any participant who initiated injection drug use over the study period was included at the first follow-up where injection drug use was reported. Further, to assess for injection cessation, only participants who completed at least one subsequent study visit after a report of active injection drug use were considered for the analysis.

To examine patterns of non-injection drug use from periods of active injection to periods of injection cessation, we considered the following self-reported measures of non-injection drug use: crack/cocaine use; crystal methamphetamine use; heroin use; and cannabis use. We examined two dichotomized variables for each non-injection drug use measure: any use in the previous six months (at least once vs. none); and daily use in the previous six months (at least once/day vs. none). We defined injection cessation based on responses to the question: "In the last six months, when you were using, which of the following drugs did you inject, and how often?" Participants who reported not having injected any drugs following at least one previous report of active injection drug use were considered cases. Participants who did not cease injecting drugs over the study period were considered controls. For each cessation case, the injection cessation period was defined as the six-month period referenced in the study visit where no injection drug use was reported. The active injection period was defined as the six-month period referenced in the study visit preceding the injection cessation event. Cases could experience more than one cessation event.

We also considered potential demographic, social, and drug-related exposures that could potentially differ between cases and controls including: age; years of injection experience (per additional year); gender (female vs. male); ethnicity (Caucasian vs. other); regular employment (yes vs. no); homelessness, defined as having no fixed address, sleeping on the street, or staying in a shelter (yes vs. no); DTES residency, defined as residing or, for homeless or marginally housed youth, spending the majority of time in the DTES (yes vs. no); daily injection drug use (yes vs. no); crystal methamphetamine injection (yes vs. no); heroin injection (yes vs. no); crack/cocaine injection; high-risk alcohol use (defined as exceeding the National Institutes on Alcohol Abuse and Alcoholism's definition of drinking at low-risk for developing alcohol use disorder: >14 drinks per week or >4 drinks per day for men, and >7 drinks per week or >3 drinks per day for women;[38] yes vs. no); methadone maintenance treatment (yes vs. no); non-methadone-based addiction treatment including detoxification services, out-patient treatment, and counseling services (yes vs. no); incarceration, defined as being in detention, prison, or jail (yes vs. no); sex work, defined as exchanging sex for money, drugs, or other material possessions (yes vs. no); and drug dealing (yes vs. no). All measures were self-reported, and, with the exception of gender and ethnicity, correspond to exposures in the previous six months.

Analysis

Baseline comparisons

First, we characterized the study sample at baseline using chi-square tests (categorical variables) and Mann-Whitney U tests (continuous variables) to compare baseline exposures

according to whether or not the participant ceased injecting over the study period (i.e., cases vs. controls).

Within-group changes from injection to injection cessation

As cases could potentially experience more than one cessation event (e.g., cease, relapse, cease), we examined the data at the event level, and conducted a sensitivity analysis using the first event of injection cessation. Each cessation event consisted of a pair of observations from an active injection period (i.e., the six-month period referenced in the study visit preceding the report of cessation) and a cessation period (i.e., reporting cessation in the previous six-month period). We used McNemar's test to compare within-group changes in non-injection drug use from the active injection period to injection cessation period.

Within-group changes among matched controls

In order to account for potential changes in drug use patterns in the cohort over time, we also examined changes in non-injection drug use among individuals who did not cease injection (i.e., controls). Similar to case events described above, we created control "events", consisting of a pair of observations from two consecutive follow-up periods in which the participant reported injecting drugs. These control events were matched to case events via the six-month follow-up periods corresponding to active injection and injection cessation, respectively, in case events. For example, a participant who reported injecting drugs in the six-month follow-up periods corresponding to December 2008 – May 2009 and June 2009 – November 2009 would be an eligible control event match for a case participant who reported injecting drugs during the six-month follow-up period corresponding to December 2008 – May 2009, and ceased injection drug

use for the previous six-month period corresponding to May 2009 – November 2009. For each case event, we randomly selected two control events from the pool of time-matched eligible controls, without replacement (i.e., after a control event was selected from the pool of eligible matched controls, it was ineligible to be selected as a control for another time-matched event case). McNemar's test was used to examine within-group changes in non-injection drug use patterns from the first six-month injection period to the second six-month injection period. To maximize the stability of our control estimates, we used a bootstrapping method in which we repeated control selection and McNemar's test 50 times for each case (removing any duplicate control follow-up pairs for each case follow-up pair), and reported results as a summary (i.e., average) of 50 runs.

Between-group differences in case and control changes

To determine whether the changes in non-injection drug use patterns from active injection to injection cessation differed significantly than matched controls, we built linear growth curve models,[39] adjusting for all variables that differed between case and control events in the active injection period at $p<0.10$. These differences were estimated through generalized estimating equations to account for multiple observations among individuals who ceased injecting more than once, and for repeated measures among controls. In the multivariate linear growth curve models, the slope represents the change in non-injection drug use pattern by group (i.e., case or control) over time (active injection vs. cessation period), and the *p*-value corresponds to the significance of the interaction term. Variations of this method have been previously used in studies of PWUD to compare between-group differences in within-group changes over time.[40-42] However, we have built on these previous approaches by employing a

bootstrapping method to summarize results (i.e., slope estimates and 95% confidence intervals) from 50 runs (see description above). All tests of significance were two-sided with significance fixed at $\alpha = 0.05$, and performed using RStudio Version 0.99.892 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between September 2005 and May 2015, of 1209 ARYS participants, 545 (45.1%) reported injecting drugs at baseline or during at least once during study follow-up. Of those, 387 (71.0%) participants were seen more than once and were included in this analysis. Compared to the analytic sample, participants excluded for insufficient follow-up were more likely to inject crack/cocaine at baseline (42.4% vs. 30.2%, $p = 0.005$), but did not differ from the analytic sample in terms of demographic characteristics or other types of drugs injected. In total, the study sample contributed 1976 analytic observations to the analysis. Table 1 summarizes the baseline characteristics of the sample, stratified by injection cessation over the study period. The most commonly injected drug at baseline was heroin (n = 261; 67.4%), closely followed by crystal methamphetamine (n = 235; 60.7%), then crack/cocaine (n = 117; 30.2%). In addition, 325 (84.0%) participants reported cannabis use at baseline. Participants who went on to cease injection drug use for at least one six-month period were less likely at baseline to report daily drug injection, any crystal methamphetamine injection, and any heroin injection, and were more likely to report daily use of crack or cocaine (all $p<0.05$). At baseline, those who ceased injecting at least once were also less likely to be on methadone maintenance treatment or any non-methadone form of addiction treatment (both $p<0.05$).

[Insert Table 1 here]

Overall, 173 (44.7%) participants reported ceasing injection drug use for at least one six-month follow-up period, yielding a total of 201 cessation events. The use of non-injection drugs occurred during 79.6% (n = 160) of injection cessation periods, and occurred daily during 53.7% (n = 108) injection cessation periods. Table 2 summarizes non-injection drug use patterns among cases and controls, for active injection and cessation periods. As shown, significant decreases in non-injection crack/cocaine use (any and daily), crystal methamphetamine use (any), heroin use (any) and cannabis use (any) were observed among cases following shifts from active injection to injection cessation periods (all $p<0.001$). Over the same study follow-up period, significant decreases were also observed in crack/cocaine use (any) and cannabis use (any) among matched controls (youth who continued injecting over the same period) summarized over 50 runs. Interestingly, the proportion of cases reporting daily non-injection heroin use did not change during transitions away from injection ($p = 1.00$). The only increase in non-injection drug use observed among either cases or controls was a slight increase (37.3% to 41.3%) in daily cannabis use among cases following shifts to injection cessation, compared to a slight average decrease (34.1% to 31.9%) over the same study follow-up periods among controls. Neither of these within-group changes reached statistical significance.

[Insert Table 2 here]

When we compared changes in non-injection drug use from periods of injection to injection cessation among cases to corresponding follow-up periods among controls, controlling

for group differences during the active injection (i.e., "pre-cessation") period (Table 3), we found that the decrease in daily crack/cocaine use among cases was significantly more than the decrease among controls (average *p*-value = 0.024). No other between-group changes in non-injection drug use were found to be statistically significant.

[Insert Table 3 here]

We also removed any secondary cessation events and examined the first (if not only) cessation event per case. In these analyses, we also observed decreases in daily crack-cocaine (average $p = 0.026$), but not other non-injection drug use pattern, to be significantly greater for cases than controls (data not shown).

DISCUSSION

In this study of street-involved youth who inject drugs, we observed that six-month cessation of injection was common with 45% of participants reporting cessation at least once over a 10-year period (September 2005 and May 2015). This proportion is higher than an estimate of 29% over an eight-year period among young people who inject drugs (PWID) in San Francisco, USA with the same median age,[43] but substantially lower than a 70% estimate recorded among PWID (median age: 34) in Baltimore, USA over a similar length of study period.[44] The proportion of individuals reporting non-injection drug use generally decreased following the shift from the active injection to injection cessation, yet the prevalence of non-injection drug use remained relatively high following injection cessation. Overall, non-injection

of at least one drug following injection cessation occurred for over three-quarters of cessation events.

To our knowledge, this is the first study to examine changes in non-injection drug use that accompany transitions out of injection drug use among youth. Our study was novel in that it used matched controls to examine the extent to which observed changes would have likely occurred in the cohort in the absence of injection cessation. Interestingly, when changes in non-injection drug use trends among cases and controls were compared, only daily non-injection use of crack/cocaine was found to decrease significantly more than controls from periods of active injection to injection cessation. This finding is particularly promising considering prior research that has pointed to non-injection cocaine use as a significant predictor of relapse to injection drug use after injection cessation.[44] Overall, however, our findings demonstrate that although cessation of injection drug use occurs regularly, it is often in the context of continued use of non-injection drugs. Furthermore, continued engagement in lower risk (i.e., non-injection) drug use during cessation of injection suggests an important harm reduction opportunity, suggesting that at-risk youth may benefit from models of substance use care that operate from or incorporate a harm reduction philosophy. Specifically, as abstinence-based models are still the norm in many youth addiction treatment services,[24] these findings lend support to the notion that youth treatment models should consider a range of pathways to wellness including expanding strategies that can help youth transition to safer forms of drug use without requiring abstinence as the sole objective. This recommendation is consistent with prior research suggesting that abstinence from all substance use may not be common among many street-involved youth,[45] and is made with

careful consideration of the frequent shortcomings (e.g., drop-out, relapse)[21-24] and risk of harm (e.g., overdose)[25-28] associated with abstinence-oriented treatment models.

In light of descriptive studies among other populations, including medical and non-medical cannabis users in California that have demonstrated cannabis use as a substitute for illicit drugs,[31,46] we were interested in potential increases in cannabis use during injection cessation periods. In our study, which examined aggregate-level trends in cannabis use, we noted that daily cannabis use was the only non-injection drug use pattern to increase among cases in the follow-up period corresponding to injection cessation; however these changes were not statistically different from controls.

Findings from our study should be interpreted in the context of certain limitations. Since it is not possible to generate a random sample of hard-to-reach populations such as street-involved youth, our findings cannot be generalized to all street-involved youth who inject drugs in Vancouver or in other settings. We also relied on self-reported measures of drug use and other sensitive personal information, which is subject to response bias including social desirability bias. However, we have no reason to suspect that respondent accuracy on patterns of drug use would differ according to injection cessation status or cessation period. Recognizing that non-medical use of pharmaceutical opioids remains a prevalent trend among some populations of at-risk youth,[47] and has been linked to injection initiation,[48] we had also intended to examine changes in non-injection use of pharmaceutical opioids during transitions to injection cessation. However, relatively low cell counts for daily and any non-injection pharmaceutical opioid use prevented us from including this data in the present analysis. Finally, we cannot overlook the

possibility that youth who cease all illicit drug use may be less likely to return for subsequent study visits, potentially reducing the estimated proportion of cases who ceased non-injection drug use. Nevertheless, we did note that there were few differences at baseline between those who were retained in our study and those who were excluded for a lack of follow-up.

With the exception of daily use of crack/cocaine, decreases in non-injection drug use following shifts to injection cessation among our sample do not differ significantly from youth who continue to inject. While transitioning out of injection drug use occurred for almost half of our sample, these transitions were largely accompanied by continued use of drugs through lower risk modes of administration. Given that these shifts represent significant reductions in risks for drug-related harm, our findings suggest that novel strategies promoting safer substance use and transitions away from injecting should be urgently evaluated. These programs may compliment traditional abstinence-based approaches that may not be suitable for all youth. Treatment and care models focused on at-risk youth should specifically consider broadening their objectives and expanding services to reach those not ready to abstain from all modes and types of drug use but who may be ready and willing to shift to less risky forms of substance use.

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