

ABSTRACT

Background: Despite the popularity of MDMA (ecstasy) among young people across North America and Europe, MDMA is rarely explored in studies of young people at high-risk of injecting drugs. We conducted a study among street-involved youth who use illicit drugs in Vancouver, Canada to understand if use of MDMA is associated with initiation of injection drugs.

Methods: We followed injection-naïve participants in the At-Risk Youth Study (ARYS), an ongoing prospective cohort of street-involved youth who use illicit drugs aged 14-26. Bivariate and multivariate extended Cox models with time-updated variables were used to examine the association between MDMA use and initiation of injection drug use between September 2005 to May 2015.

Results: Among 483 youth, 306 (63.4%) had a history of MDMA use and 218 (45.1%) had used MDMA in the previous six months at baseline. A total of 105 (21.7%) youth initiated injection drug use over the 10-year period, yielding an incidence density of 8.51 (95% Confidence Interval [CI]: 6.96 – 10.30) per 100 person-years. MDMA use was not significantly associated with initiating injection drugs at the bivariate- (Hazard Ratio: 0.93; 95% CI: 0.61 – 1.42) or multivariate- (Adjusted Hazard Ratio: 0.88; 95% CI: 0.57-1.35) level after adjusting for unemployment, homelessness, and crystal methamphetamine use.

Conclusions: Amid ongoing frequent use of MDMA among some young people in North America, we did not observe an elevated risk of injection initiation among those who used MDMA in this cohort of street-involved youth.

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Keywords: N-Methyl-3,4-methylenedioxyamphetamine, MDMA, ecstasy, injection drug use, youth, adolescent

INTRODUCTION

3,4-Methylenedioxymethamphetamine (MDMA) – more generally known as ‘ecstasy’ or ‘molly’ – is commonly used among certain youth and young adult populations in North America,^{1,2} and is thought to be gaining popularity in several European Union (EU) countries.³ Specifically, its use is common in electronic music settings including nightclubs and festivals, where recent estimates suggest a lifetime prevalence of over 40% among attendees.⁴ It has been suggested that growing usage rates in certain EU countries mark an evolution from niche nightlife and music scenes to more mainstream settings such as bars and parties.³ Across general population demographics, MDMA is estimated to be used by 4-5% of senior high school students in Canada and the United States,^{5,6} 13% of young adults (aged 18-25) in the US,⁷ and 4.2% of adults in the EU.³ MDMA is known for its ability to invoke pro-social effects (e.g., enhance feelings of empathy, social connectedness and improve interpersonal relationships).⁸ In the 1970’s, MDMA was used experimentally by some psychiatric professionals to improve patient communication during psychotherapy.⁹ Since 2011, research has been ongoing to establish the safety and efficacy of MDMA as an adjunct to psychotherapeutic treatment of illnesses such as post-traumatic stress disorder (PTSD).¹⁰⁻¹²

Despite its medical roots, the recreational use of MDMA – or, as is often the case, substances marketed as MDMA containing other compounds – can cause harmful adverse health effects including overheating and dehydration, especially if used with other substances.⁹ Previous observational research among youth or young adult populations identify links between MDMA use and other substance use, including alcohol, tobacco, cannabis, and other illicit drugs.² In a survey of MDMA-using young adults in the US, earlier onset of MDMA use (as well as alcohol and cannabis use) was associated with earlier onset of cocaine and methamphetamine use, spurring discussions around MDMA’s role along the ‘gateway’

sequence to higher-risk drug use, due to the common perception by young people that it is a low-risk form of drug use.¹³

Public health priorities continue to emphasize the importance of intervening early in the trajectory of substance use among adolescents and young adults to reduce the risk of problematic use or associated harms.¹⁴ In particular, given extensive morbidity and mortality associated with injection drug use,^{15,16} preventing or delaying the initiation of injection drug use is critical. Cross-sectional research in Australia estimates that almost one-quarter of people who regularly use MDMA have a history of injection drug use, and roughly 15% are thought to be recent injectors,¹⁷ but it is unclear if MDMA use is associated with initiation of injection drug use. Despite the ongoing popularity of MDMA among younger populations in North America, and particularly among street-involved young people,¹⁸ we are not aware of any research examining the relationship between MDMA use and initiation of injection drug use in these settings. We aimed to investigate the association between MDMA use and initiation of injection drug use among street-involved youth in a Canadian setting.

METHODS

Participants

Data for this study was derived from the At-Risk Youth Study (ARYS), an ongoing prospective cohort of street-involved youth and young adults who use illicit drugs. This study has been described in detail previously.¹⁹ 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 between 14 and 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.^{20,21} Since the outcome of interest in this particular study was initiation of injection drug use, the current analysis was restricted to ARYS participants who had no history of injection drug use at study entry, and who completed at least one subsequent study follow-up to assess for injection initiation.

Procedure

At baseline and bi-annually, participants completed an interviewer-administered questionnaire eliciting information on time-updated socio-demographic, behavioural, and health-related exposures. Each participant also underwent a consultation with a study nurse, and were referred to appropriate health care services if needed. All participants received 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

The outcome was time to injection initiation, estimated from the participant’s baseline survey to the mid-point between the date of the last follow-up interview in which they did not report injecting drugs and the date of the first follow-up interview in which they reported injecting drugs. This definition is consistent with prior studies of injection initiation.^{22,23} At each interview, participants were asked: ‘In the last six months, when you were using, which of the following non-injection drugs did you use?’ MDMA use was measured as a binary variable (yes vs. no), indicated by a positive or negative response to the use of ‘Ecstasy’ (the common name for psycho-stimulant drugs assumed to contain MDMA).¹⁸

We included the following socio-demographic characteristics hypothesized to influence a potential association between MDMA use and injection initiation: age (in years), gender (male vs. female); ethnicity (White vs. other); high school completion (yes vs. no); recent employment, defined as holding a regular job, self-employment, or temporary work as a source of income in the previous six months (yes vs. no); recent homelessness, defined as having no fixed address, sleeping on the street, or staying in a shelter in the previous six months (yes vs. no); recent Downtown Eastside (DTES) residency, defined as residing or – for homeless or marginally housed youth – spending the majority of time in the DTES in the previous six months, (yes vs. no); and recent engagement in sex work, defined as exchanging sex for money, gifts, food, shelter, clothes, drugs, or favours at least once in the previous six months (yes vs. no). As drug use trends may change as a function of time with changes in market availability or social norms, we also included a variable for year of study.

Considering that poly-substance use is common in this population, we also included several substance use patterns which may be associated (either positively or negatively) with MDMA use and which may influence transitions into injection drug use. We included a measure for heavy alcohol use, defined as consuming >14 drinks per week or >4 drinks per day for males, and >7 drinks per week or >3 drinks per day for females. We chose these cut-offs to match the upper thresholds for drinking at a ‘low risk’ of developing an alcohol use disorder, as defined by the National Institute on Alcohol Abuse and Alcoholism.²⁴ We also included measures for cannabis use, crack/cocaine use, crystal methamphetamine (CM) use, heroin use, and non-medical pharmaceutical opioid use in the previous six months, which were self-reported and coded as binary (yes vs. no). Consistent with other studies of injection initiation,^{23,25} all substance use variables, including those for MDMA, refer to the six-month period in the follow-up preceding the outcome assessment to prevent erroneously interpreting a post-injection drug use exposure as a pre-injection exposure.

Statistical analysis

First, we examined sample characteristics at baseline. We used Chi-square tests (Wilcoxon rank-sum test for age) to compare study characteristics between participants who did and did not report MDMA use at baseline. Next, we estimated the relative hazard of initiating injection drug use with bivariate and multivariate extended Cox models accounting for the time-updated nature of study variables. To assess the relationship between MDMA use and time-to injection initiation, MDMA use was included in the multivariate analysis, along with all variables associated with injection initiation at $p < 0.10$ in bivariate analysis. All p-values are two-sided with significance fixed at $\alpha = 0.05$. Statistical analyses were performed using RStudio 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between September 2005 and May 2015, 683 injection-naïve participants were interviewed, and 483 (70.7%) returned for at least one study follow-up and were included in the analysis. Compared to participants who were ineligible due to insufficient follow-up, the study sample had a slightly higher median age (21.5 years vs. 20.7 years, $p = 0.029$) and reported more non-injection crack or cocaine use at baseline (76.0% vs. 62.0%, $p < 0.001$). All other variables under study, including MDMA use, did not differ significantly at baseline. In total, these 483 study participants contributed 2347 observations to the study. The median number of follow-ups per participant was 4 (Interquartile range [IQR]: 2 – 6) and the median follow-up time per participant was 22.5 (IQR: 12.8 – 42.9) months. In total, 149 (30.8%) women were included in this study. The majority of participants reported white ($n = 294$; 60.9%) or Indigenous ($n = 125$; 25.9%) ethnicity. The rest of the sample included black (5.2%), other (including Asian, south Asian, and Latino; 4.8%) or mixed-ethnicity (1.9%).

At baseline assessment, 306 (63.4%) youth reported having ever used MDMA and 218 (44.8%) reported using it in the previous six months. Baseline characteristics of the sample stratified by recent MDMA use are shown in Table 1. Those who reported recent MDMA use had a younger median age (20.9 years vs. 21.9 years, $p < 0.001$), and were less likely to engage in sex work (4.7 vs. 9.7%, $p = 0.034$). In terms of substance use patterns, these participants were more likely to use cannabis (96.8% vs. 86.8%, $p < 0.001$), engage in higher-risk alcohol consumption (57.3% vs. 34.1%, $p < 0.001$), and use pharmaceutical opioids non-medically (17.9% vs. 5.0%, $p < 0.001$) in the previous six months. The median year of baseline interview was significantly higher for participants who used MDMA (2009; IQR: 2006-2009) than participants who did not use MDMA (2006; IQR: 2006-2009).

In total, 105 (21.7%) youth initiated injecting drugs over 1233.8 person-years of risk, resulting in an incidence density of 8.51 (95% confidence interval [95% CI]: 6.96 – 10.3) per 100 person-years. As shown in Table 2, at the bivariate level, characteristics associated with initiating injection drug use were: employment (Hazard Ratio [HR]: 0.40, 95% CI: 0.27 – 0.62); homelessness (HR: 2.23, 95% CI: 1.48 – 3.36); DTES residency (HR: 1.77, 95% CI: 1.18 – 2.64); non-injection use of CM (HR: 2.52, 95% CI: 1.70 – 3.73); and non-injection use of heroin (HR: 2.08, 95% CI: 1.33 – 3.26). In multivariate analysis (Table 2), employment (Adjusted Hazard Ratio [AHR]: 0.49, 95% CI: 0.32 – 0.76), homelessness (AHR: 1.87, 95% CI: 1.22 – 2.86), and non-injection CM use (AHR: 2.41 (95% CI: 1.60 – 3.62) remained significantly associated with initiating injection drug use (all $p < 0.05$). MDMA use was not significantly associated with initiating injection drug use in bivariate (HR: 0.93, 95% CI: 0.61 – 1.42) or multivariate (AHR: 0.91, 95% CI: 0.59 – 1.40) analyses ($p > 0.05$).

DISCUSSION

In this study, we explored the relationship between MDMA use and initiation of injection drug use over a 10-year period in a cohort of highly susceptible youth. Almost half of participants reported recent use of MDMA at baseline; for comparison, past-year use among Canadians attending high school is 2.6%.⁶ Despite this comparatively high usage rate, we did not find evidence that MDMA use accelerates transitions to injection drug use in this sample of at-risk youth. Based on an examination of baseline characteristics, we note certain patterns that may help explain this lack of association. As confirmed in the present analysis, CM use is a well-documented risk factor for injection initiation among this population of street-involved youth.^{26,27} Previous research in this setting suggests that CM is the first drug injected for 25-50% of initiates, after having transitioned from CM snorting or smoking.^{26,27} Although 42% of participants in this study who used MDMA at baseline reported recent CM use, this prevalence is comparatively lower than the estimated 81% of people who use MDMA regularly in cities in Australia,²⁸ and it was not significantly different than that for participants who reported no MDMA use at baseline. Similarly, those who reported MDMA use did not report increased non-injection use of other drugs commonly used to initiate injection drug use, including heroin and crack/cocaine.^{29,30} Almost all (>95%) participants using MDMA at baseline were also using cannabis, which has been previously linked to a reduced likelihood of injection initiation in this setting³¹ and among populations of people who use drugs in other settings.³² MDMA was also found to be associated with heavy alcohol consumption and non-medical pharmaceutical opioid use at baseline. Findings from previous studies conducted among a nationally representative sample of youth and young adults³³ and young MDMA users¹³ have suggested that MDMA use in adolescence or early adulthood is a predictor of future high-risk drug use including cocaine, methamphetamine, and heroin. However, against the current study landscape in which youth are regularly exposed to illicit drugs and an open injection drug use scene, our findings suggest

that MDMA use may occur in close temporal proximity to other substances generally initiated in earlier stages of illicit drug use trajectories (i.e., alcohol, cannabis, and pharmaceutical opioids),^{34,35} without being implicated in the acceleration of these trajectories towards injection.

The present study offers guidance to clinicians and social service providers on whether youth who use MDMA represent a target population for injection initiation prevention efforts. The main finding presented here suggests that among a population of street-involved youth with frequent exposure to injection drug use, MDMA use was not found to be an indicator of high risk for injection. That MDMA use was not observed to increase the likelihood of injection initiation is notable given the current renaissance of psychotherapeutic research involving MDMA for PTSD. History of personal trauma, including childhood abuse and neglect, is extremely high among street-involved youth³⁶ and has been linked with earlier initiation of injection drugs³⁷ and quicker progression to regular injection drug use.³⁸ Future research should explore the possible psychotherapeutic use of MDMA among street-involved youth suffering from the effects of trauma and adverse childhood events in this setting.

Secondary findings from this study illustrate other factors predisposing young people to use injection drugs in this setting. We observed that experiencing unemployment and homelessness were significantly associated with initiating injection drugs. These findings, which provide time-updated support of previous research in this setting,^{25,39} underline the transition to injection drugs as one of the many pathways through which structural vulnerabilities contribute to poorer health among drug using populations.⁴⁰ Finally, the use of CM was significantly associated with shorter time to injection initiation in this study. As discussed above, this association has been well established and highlights an important area for intervention efforts.

Our findings should be interpreted in light of certain limitations. First, all substance use patterns, including MDMA use, were ascertained through self-report, which may have introduced instances of insufficient recall, responding according to social norms and desires,

and under-reporting of MDMA use since the newer term 'molly' – often in reference to MDMA in powder form – was not included in our study questionnaire.⁴¹ Second, ARYS is not a random sample of street-involved youth, which may limit the generalizability of these findings. Third, MDMA used for recreational purposes is not regulated and is frequently adulterated with other compounds (e.g., paramethoxymethamphetamine⁴² or synthetic cathinones – i.e., 'bath salts'),⁴ thus any reference to MDMA/'ecstasy' in this study cannot be assumed to be pure MDMA.

In summary, amid the ongoing popularity of MDMA among young people, we did not find evidence that MDMA use encourages transitions to injection drug use within a cohort of street-involved young people. Although MDMA use is not in and of itself an indicator of accelerated transitions to higher risk modes of drug administration in this study, this population of street-involved youth, in which MDMA use is substantially higher than average, contends with several other social and structural vulnerabilities that should be addressed in efforts to reduce the incidence of injection initiation.

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