DRUG USE PATTERNS PREDICT RISK OF NON-FATAL OVERDOSE AMONG STREET-INVOLVED YOUTH IN A CANADIAN SETTING

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Abstract

Background—Non-fatal drug overdose is a major cause of morbidity among people who use drugs, although few studies have examined this risk among street-involved youth. We sought to determine the risk factors associated with non-fatal overdose among Canadian street-involved youth who reported illicit drug use.

Methods—Using data from a prospective cohort of street-involved youth in Vancouver, Canada, we identified youth without a history of overdose and employed Cox regression analyses to determine factors associated with time to non-fatal overdose between September 2005 and May 2012.

Results—Among 615 participants, 98 (15.9%) reported a non-fatal overdose event during follow-up, resulting in an incidence density of 7.67 cases per 100 person-years. In multivariate Cox regression analyses, binge drug use (adjusted hazard ratio [AHR] = 1.85; 95% confidence interval [CI] = 1.20 – 2.84), non-injection crystal methamphetamine use (AHR = 1.70; 95% CI = 1.12 – 2.58), non-injection prescription opiate use (AHR = 2.56; 95% CI = 1.36 – 4.82), injection prescription opiate use (AHR = 2.49; 95% CI = 1.40 – 4.45) and injection heroin use (AHR = 1.85; 95% CI = 1.14 – 3.00) were positively associated with time to non-fatal overdose. Social, behavioural and demographic factors were not significantly associated with time to non-fatal overdose event.

Conclusions—Rates of non-fatal overdose were high among street-involved youth. Drug use patterns, in particular prescription opiate use, were associated with overdose. These findings underscore the importance of addiction treatment and prevention efforts aimed at reducing the risk of overdose among youth.

INTRODUCTION

Individuals who use illicit drugs face considerable risk of accidental overdose, and drug overdose mortality has emerged as a leading cause of accidental death in North America (Kerr et al., 2007; Pollini et al., 2006; Sergeev et al., 2003). Non-fatal drug overdose is also associated with significant morbidity related to physical injuries, aspiration pneumonia, renal failure, and hypoxic brain injury (Warner-Smith et al., 2002).

Among adults, drug use characteristics such as heroin injecting (Fairbairn et al., 2008) and polysubstance use (Davidson et al., 2003) have been found to be important predictors of non-fatal overdose. Concurrent use of sedatives such as alcohol and benzodiazepines are also associated with increased likelihood of overdose (Darke et al., 1996; Dietze et al., 2005), and heavy alcohol use has been linked to an increased risk of mortality in this context (Hser et al., 2001).

Unfortunately, much of the research focused on identifying risk factors for non-fatal drug overdose has examined adult populations (Fairbairn et al., 2008; Kerr et al., 2007; Seal et al., 2001), and risk factors for non-fatal overdose among street-involved youth have not been as well described. This is despite an association between younger age and increased risk of overdose (Coffin et al., 2007; Fairbairn et al., 2008; Seal et al., 2001). The majority of research studies concerning youth drug overdose have examined heroin use (Sergeev et al., 2003; Sherman et al., 2007), and few longitudinal studies have investigated the influence of prescription drug misuse (Silva et al., 2013). This gap in research is of concern, since drug overdoses have been identified as an important cause of preventable death among street-involved youth (Roy et al., 2004) and are increasing in prevalence (White et al., 2011; Fischer et al., 2014).

Although drug overdose among street-involved youth is a growing epidemic in North America (Boivin et al., 2005), few prospective studies have examined risk factors for overdose among this population. Therefore, the present longitudinal study was conducted to characterize the risk factors associated with non-fatal overdose among a cohort of street-involved youth in a Canadian setting where a range of different illicit drugs are commonly used.

2. MATERIAL AND METHODS

The present study employed data from the At-Risk Youth Study (ARYS), a prospective cohort study of street-involved youth aged 14 and 26 years living in Vancouver, Canada (Wood et al., 2006). Cohort participants are recruited through extensive street-based outreach, various community services, and self-referral, using a combination of snowball and convenience sampling. Efforts to ensure a representative sample included outreach in a range of neighbourhoods, during the day and night-time, with attempts also made to have participants recruit their peers.

To be eligible for inclusion, participants need to be between 14 and 26 years old at the time of enrollment, report using an illicit drug other than or in addition to marijuana in the 30 days prior to enrollment, and be 'street-involved' defined as having been temporarily or absolutely without housing in the preceding six months, or having accessed street-based youth services during that time. All participants provide written informed consent prior to joining the study.

At baseline and semi-annual follow-up visits, participants complete an interviewer-administered questionnaire that inquires about demographic and socio-economic information, and drug use behaviours. At each study visit participants receive a $20 CAD (Canadian Dollars) honorarium. The study has had ethics approval by the University of British Columbia/Providence Health Care Ethics Review Board.

Data were collected from participant interviews conducted between September 2005 and May 2012. The outcome of interest was defined as the self-report of at least one incident of non-fatal drug overdose in the past six month period. Specifically, we asked participants "In the last six months, have you ever overdosed by accident (i.e. where you had a negative reaction from using too much drugs)?"

A number of variables were explored as potential predictors of non-fatal overdose in our study. Demographic variables included: age (per year older), gender (male vs. female), and ethnicity (Caucasian vs. other). Behavioural variables included: assisted injection, defined as having received manual assistance with the injection process from another individual (yes vs. no); public injection, defined as injecting in city streets, parks and alleys (yes vs. no); rushed public injection, defined as feeling rushed when injecting drugs in public areas (yes vs. no). Given that safer injection education may involve overdose prevention messaging and information about reversal methods, we considered whether participants had ever been taught safer injection techniques by a health care provider (yes vs. no). Social variables included: engagement in sex work, defined as having exchanged money, gifts, drugs or something else of value for sex (yes vs. no); police encounters, defined as recently having been stopped, searched or questioned by police (yes vs. no); homelessness, defined as having no fixed address, sleeping on the street, couch surfing, or staying in a shelter or hostel (yes vs. no); and residence in the 'Downtown Eastside' (DTES), which is Vancouver's drug use epicenter (yes vs. no) (Kerr et al., 2003). Drug use variables that were explored included: heavy alcohol use (based on National Institute on Alcohol Abuse and Alcoholism definitions for males [more than 4 drinks per day or more than 14 drinks per

week] and females [more than 3 drinks per day or more than 7 drinks per week]) (yes vs. no) (NIAAA, 2015); non-injection crystal methamphetamine use (yes vs. no); crystal methamphetamine injection (yes vs. no); non-injection heroin use (yes vs. no); heroin injection (yes vs. no); non-injection prescription opiate use (yes vs. no); prescription opiate injection (both prescription opiate use variables included illicit methadone, morphine, oxycodone, Dilaudid [hydromorphone], Percocet [acetaminophen and oxycodone], Demerol [meperidine], fentanyl, Vicodin [hydrocodone] Talwin (pentazocine), and Tylenol 3 [codeine]) (yes vs. no); crack cocaine smoking (yes vs. no); non-injection cocaine use, defined as any intranasal use (yes vs. no); and cocaine injection (yes vs. no). We also included a measure of binge drug use; specifically, we asked participants, "In the past six months, did you go on runs or binges (that is, when you used non-injection/injection drugs more than usual)?" (yes vs. no).

All behavioural, social and drug use variables refer to activities in the previous six months, with the exception of being taught safer injection practices, which referred to education occurring "ever".

To assess factors associated with time to first overdose event during the study period, all ARYS participants who had completed at least one follow-up questionnaire and had not reported an overdose incident in the past six months at baseline were included in the analysis. The time to first overdose event was defined as the time interval between recruitment into the cohort and estimated date of this non-fatal overdose. Persons who never reported an overdose during follow-up were right-censored at the interview date of their last study visit.

Baseline characteristics of study participants were stratified according to gender, given past studies have shown gender differences in overdose patterns (Coffin et al., 2007; Werb et al., 2008). The counting process framework was used for applying the bivariate and multivariate Cox regression in this analysis. For the multivariate Cox analyses, variables being significant at $p < 0.05$ in the bivariate Cox analyses were considered. The Akaike Information Criterion (AIC) model building approach for variable selection was used to select the best multivariate model, as indicated by the lowest AIC value (E.S. Shtatland, 2001).

All statistical analyses were performed using the SAS software version 9.3 (SAS Institute Inc., Cary, NC). All p values are two-sided.

3. RESULTS

Between September, 2005 and May, 2012, 1019 street-involved youth were recruited into the ARYS cohort. Of the 1019 street youths recruited, 615 (60.4%) did not report a recent non-fatal overdose event at enrollment and had returned for at least one follow-up visit. Of the 615 participants, 421 (68.5%) were male, 403 (65.5%) reported being Caucasian, and the median age was 21 years (interquartile range [IQR] = 20 – 23). Compared to the 404 individuals who were not eligible for the primary analysis, the study sample of 615

participants were less likely to be Caucasian (65.5% vs. 72.3%, p = 0.026). There were no significant differences in age and gender.

Table 1 presents baseline characteristics stratified by gender. Over study follow-up, a total of 98 (15.9%) of these participants reported at least one incident of non-fatal overdose, resulting in an incidence density of 7.67 cases (95% confidence interval [CI] = 6.15 – 9.19) per 100 person-years.

Table 2 presents the results of the bivariate and multivariate Cox regression analyses. In multivariate analysis, factors that were significantly associated with time to non-fatal overdose during the study period included: binge drug use (adjusted hazard ratio [AHR] = 1.85; 95% CI = 1.20 – 2.84); non-injection crystal methamphetamine use (AHR = 1.70; 95% CI = 1.12 – 2.58); non-injection prescription opiate use (AHR = 2.56; 95% CI = 1.36 – 4.82); prescription opiate injection (AHR = 2.49; 95% CI = 1.40 – 4.45); and heroin injection (AHR = 1.85; 95% CI = 1.14 – 3.00).

4. DISCUSSION AND CONCLUSIONS

The present longitudinal study demonstrates that non-fatal overdose was relatively common among street-involved youth in this Canadian setting although not as prevalent as figures reported among some samples of heroin injecting youth in the United States (Seal et al., 2001; Ochoa et al., 2005). In multivariate Cox analyses, non-fatal overdose was independently and positively associated with binge drug use, as well as specific forms of drug use including patterns of non-injection and injection opiate and stimulant drug use.

Multiple drug use behaviours were independently associated with a risk of non-fatal overdose. Specifically, injection heroin use was strongly associated with non-fatal overdose in the present study; this is consistent with previous research (Kerr et al., 2007; Werb et al., 2008) and highlights the importance of targeting overdose prevention interventions to young heroin users. The use of injection and non-injection prescription opiates were also found to have a strong relationship with incidence of non-fatal overdose. This is of concern as prescription opiate misuse among youth has been described as an epidemic in the U.S. (CDC, 2011), and is becoming increasingly widespread in Canada (Roy et al., 2011; King, 2014), suggesting that subsequent increases in the frequency of overdose events and related harms may also be expected. It should be noted, however, that a number of shifts in prescribing practices and drug policy have taken place which may influence the use of prescription opioids and risk of overdose among street-involved youth. Across Canada, there was an increase in the amount of opioids prescribed by physicians between 2005 – 2010 (Fischer et al., 2011), and in Vancouver there was an increase in the availability of nonmedical prescription opioids to illicit drug users (Nosyk et al., 2012). However, in 2011, the dispensing of opioids declined sharply, driven by new national opioid dispensing guidelines (NOUGG, 2010), and by the delisting of OxyContin from most provincial drug formularies in 2012 (INCB, 2013). Despite these changes, some research suggests that abuse of prescription opioids as a class has not decreased, but instead shifted to other prescription opioids such as extended-release oxymorphone (Cassidy et al., 2014).

To reduce drug overdose events and other harms associated with heroin and prescription opiate misuse, prevention efforts should be focused on increasing the availability of opioid addiction therapies for youth. Research suggests that prescription opioid users are a population more resistant to traditional harm reduction efforts (Frank et al., 2014). However there have been documented successes in preventing prescription opioid misuse in the U.S. (Spoth et al., 2013) and innovative, community-based programs are gaining favour (Frank et al., 2014). The use of suboxone (a combination of buprenorphine, a partial opioid agonist used in opioid detoxification and maintenance, and naloxone) has emerged as an approach to treat individuals with opioid addiction (SAMHSA, 2007) yet it has not been well-studied in youth (Smith, 2011). Initial research suggests that extended buprenorphine treatment might be beneficial to youth with opioid addiction (Woody et al., 2008), and further studies of opioid agonist and antagonist medications in youth are needed (Krupitsky et al., 2011). Other risk factors, such as comorbid psychiatric disorders, also need to be addressed (Katz et al., 2013). Finally, given the established successes in preventing overdose fatalities with naloxone (Clark et al., 2014), expansion of harm reduction programs that include naloxone distribution should be a priority.

Non-injection use of crystal methamphetamine was also found to be associated with non-fatal overdose events in the current study. These findings mirror research in youth and adults demonstrating a relationship between stimulant use and overdose (Davidson et al., 2003; Werb et al., 2008). Taken together, our findings highlight the need for comprehensive interventions that address the spectrum of illicit stimulant and opioid-based drug use, such as supervised injection facilities (Hadland et al., 2014).

A host of behavioural and social factors, such as public injecting, were not found to be associated with risk of non-fatal overdose in our multivariate model. These findings are surprising, as previous research has shown a relationship between public injecting and non-fatal overdose among adult drug users (Kerr et al., 2007; Kinner et al., 2012; Milloy et al., 2008). However, a previous study of risk behaviour among youth found no association between public injecting and risk of overdose among street-involved youth (Marshall et al., 2010). The difference in behavioural factors related to overdose in adult compared to youth populations warrants further study.

Our study has several limitations. As with other prospective cohort studies, ARYS is not a random sample, although efforts have been made to derive a representative sample (Wood et al., 2006). Additionally, behavioural data and drug use variables are based on self-report, and as a result it is possible that risk behaviours have been underreported in face-to-face interviews (Macalino et al., 2002), or potentially over-reported.

In summary, we found that non-fatal overdose was common among street-involved youth and associated with a range of drug use variables including binge drug use, heroin injection, prescription opiate misuse, and stimulant use whereas other behavioural and social characteristics were not associated with drug overdose events. Our results suggest that additional resources and supports, including further exploration of innovative youth-focused opiate addiction treatment strategies, are required to reduce the risk of drug overdose events among street-involved youth.

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Highlights

1. We examined the risk factors associated with non-fatal drug overdose among youth

2. Binge drug use and illicit drug use were found to be associated with risk of overdose

3. Prescription opiate use, which is increasing among youth, was also associated with overdose

4. Comprehensive interventions to address illicit and prescription drug use among youth are needed

TABLE 1

Baseline characteristics of street-involved youth who did not report recent drug overdose in Vancouver, Canada, stratified by gender ($n = 615$).

Characteristic	Total (%) (n = 615)	Gender	
		Male (%) (n =421)	Female (%) (n = 194)
Demographic factors			
Age (Median, IQR)	21 (20 – 23)	22 (20 – 23)	21 (18 – 23)
Caucasian	403 (65.5)	282 (67.0)	121 (62.4)
Behavioural and social factors			
Assisted injection	50 (8.1)	28 (6.7)	22 (11.3)
Public injection	111 (18.0)	69 (16.4)	42 (21.7)
Rushed public injection	68 (11.1)	42 (10.0)	26 (13.4)
Taught safer injection*	51 (8.3)	32 (7.6)	19 (9.8)
Sex work	59 (9.6)	26 (6.2)	33 (17.0)
Police encounters	204 (33.2)	151 (35.9)	53 (27.3)
Homeless	437 (71.1)	308 (73.2)	129 (66.5)
DTES residence	164 (26.7)	107 (25.4)	57 (29.4)
Drug use			
Binge drug use	243 (39.5)	167 (39.7)	76 (39.2)
Heavy alcohol use	245 (39.8)	175 (41.6)	70 (36.1)
Non-injection CM use	235 (38.2)	163 (38.7)	72 (37.1)
Non-injection heroin use	125 (20.3)	87 (20.7)	38 (19.6)
Non-injection prescription opiate use	48 (7.8)	35 (8.3)	13 (6.7)
Crack cocaine smoking	366 (59.5)	260 (61.8)	106 (54.6)
Non-injection cocaine use	272 (44.2)	190 (45.1)	82 (42.3)
CM injection	90 (14.6)	60 (14.3)	30 (15.5)
Heroin injection	105 (17.1)	68 (16.2)	37 (19.1)
Prescription opiate injection	45 (7.3)	23 (5.5)	22 (11.3)
Cocaine injection	44 (7.2)	30 (7.1)	14 (7.2)

Note: All behavioural, social and drug use variables refer to activities in the preceding six months (unless indicated)

Note: IQR = interquartile range; DTES = Downtown Eastside; CM = crystal methamphetamine

*Refer to activities in participant's lifetime

TABLE 2

Unadjusted and adjusted Cox regression analyses for factors associated with non-fatal drug overdose among street-involved youth in Vancouver, Canada, 2005–2012 ($n = 615$).

Characteristic	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	*p* value[*]
Demographic factors			
Age (per year older)	0.98 (0.90 – 1.06)	--	--
Male gender	0.84 (0.56 – 1.27)	--	--
Caucasian	0.98 (0.65 – 1.47)	--	--
Behavioural and social factors			
Assisted injection	2.41 (1.47 – 3.96)	--	--
Public injection	2.61 (1.72 – 3.96)	--	--
Rushed public injection	2.53 (1.56 – 4.08)	--	--
Taught safe injection[**]	1.57 (0.86 – 2.89)	--	--
Sex work	1.29 (0.59 – 2.83)	--	--
Police encounters	1.62 (1.06 – 2.47)	--	--
Homeless	1.35 (0.91 – 2.02)	--	--
DTES residence	1.22 (0.79 – 1.87)	--	--
Drug use			
Binge drug use	2.64 (1.78 – 3.93)	1.85 (1.20 – 2.84)	0.005
Heavy alcohol use	1.31 (0.88 – 1.96)	--	--
Non-injection CM use	1.93 (1.29 – 2.89)	1.70 (1.12 – 2.58)	0.013
Non-injection heroin use	1.71 (1.02 – 2.85)	--	--
Non-injection prescription opiate use	4.33 (2.44 – 7.68)	2.56 (1.36 – 4.82)	0.004
Crack cocaine smoking	1.84 (1.23 – 2.75)	--	--
Non-injection cocaine use	1.79 (1.19 – 2.69)	1.41 (0.92 – 2.17)	0.119
CM injection	2.11 (1.35 – 3.31)	--	--
Heroin injection	2.71 (1.79 – 4.10)	1.85 (1.14 – 3.00)	0.013
Prescription opiate injection	5.00 (3.02 – 8.28)	2.49 (1.40 – 4.45)	0.002
Cocaine injection	3.26 (1.97 – 5.40)	--	--

Note: All behavioural, social and drug use variables refer to activities in the preceding six months (unless indicated)

Note: HR = hazard ratio; CI = confidence interval; DTES = Downtown Eastside; CM = crystal methamphetamine

[*] *P* values for adjusted hazard ratios

[**] Refer to activities in participant's lifetime