

Determinants of overdose incidents among illicit opioid users in 5 Canadian cities

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Abstract

Background: Drug overdose is a major cause of death and illness among illicit drug users. Previous research has indicated that most illicit drug users experience nonfatal overdoses and has suggested a variety of factors that are associated with risk of overdose. In this study, we examined the occurrence of and the factors associated with nonfatal overdoses within a Canadian sample of illicit opioid users not enrolled in treatment at the time of study recruitment.

Methods: Interviewers used a standard questionnaire to collect data on sociodemographic characteristics, drug use, health and health care, experience in the criminal justice system and treatment for drug problems; they also performed standard assessments for mental health and infectious disease. The association between overdose and sociodemographic and drug-use factors was examined with χ^2 and *t* test analyses; marginally significant variables were examined with logistic regression to determine independent effects.

Results: A total of 679 subjects were interviewed; 651 provided answers sufficient for this analysis. One hundred and twelve (17.2%) of the 651 respondents reported an overdose episode in the previous 6 months. In the logistic regression analysis (after adjustment for sociodemographic factors), homelessness, noninjection use of hydromorphone in the past 30 days and involvement in drug treatment in the past 12 months were predictors of overdose ($p < 0.05$).

Interpretation: Overdose poses a considerable health risk for illicit opioid users. We found that a diverse set of factors was associated with overdose episodes. Prevention efforts will likely be more effective if they can be directed to specific causal factors.

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Populations of illicit drug users are characterized by high rates of illness and death,^{1,2} and drug overdose is a major cause of death. Studies from Australia, Europe and the United States indicate that, overall, annual rates of death due to overdose among illicit drug users are relatively stable, at about 1% to 2%.²⁻⁵ In addition, nonfatal overdose incidents are common and represent an important cause of morbidity among illicit drug users.⁶ For example, among 581 people addicted to narcotics who were admitted to the California Civil Addict Program between 1962 and 1964, there were 284 deaths

by the time of the third follow-up, 33 years later; of these, 61 (21.5%) were directly due to drug overdose or poisoning.² Other studies have provided further evidence of high rates of nonfatal overdose among illicit drug users; for example, up to two-thirds of heroin users have reportedly experienced a nonfatal overdose.⁶⁻⁸ In yet other studies, up to 89% of injection drug users surveyed reported having witnessed an overdose.⁹⁻¹¹

Epidemiologic estimates suggest that there may be as many as 100 000 injection drug users in Canada, most of whom use of illicit opioids in some form.^{12,13} Recent estimates have suggested 500 to 1000 overdose deaths per year in Canada during the past decade.¹⁴ During the 1990s, an overdose crisis developed in British Columbia, fuelled mostly by Vancouver incidents; annual overdose deaths increased substantially, from 67 in 1989 to 361 in 1993 and then to 416 in 1998, peaking at an average of more than 1 overdose death per day.^{14,15} Other data on Canadian drug user populations suggest substantial rates of overdose. Of the 1400 subjects recruited between 1996 and 2000 into the Vancouver Injection Drug User Study, 124 participants died, 41 (33.1%) because of an overdose.¹⁶ Of 776 actively injecting injection drug users in the same study, 75 (9.7%) had experienced at least 1 nonfatal overdose in the previous 6-month period.¹⁶ In a study of illicit opioid users in Toronto from 1996 to 1998 (the Smack Study), 50% of participants reported at least 1 nonfatal overdose in their lifetime, and 4% had experienced an overdose in the month before assessment.¹⁷

Research has identified a variety of risk factors for overdose. The mean age of people who experience a fatal overdose is about 30 years,¹⁸⁻²⁰ and such incidents tend to occur after several years of drug use;^{11,21} this pattern runs contrary to the popular misconception that younger, less experienced users are at greatest risk of overdose.⁵ Differences between the sexes appear nonexistent.²²⁻²⁴ There is evidence of a relation between poverty and overdose,^{19,25,26} and injection in public places (which is indicative of poor housing) is a risk factor for overdose.²⁷

Drug-use variables associated with overdose include frequency of use, and people who have overdosed on heroin report daily or almost daily use of the drug.^{7,28} Use of alcohol and benzodiazepines in conjunction with opioids is a

common characteristic of overdose incidents and is associated with greater risk.^{21,22,29,30} Administration of drugs by injection, as opposed to other routes of administration, carries the highest risk of overdose.^{5,28}

A complex risk factor for overdose is recent exposure to treatment.³¹ Drug treatment (i.e., detoxification) can lower a user's drug tolerance and increase his or her susceptibility to overdose if nonmedical drug use is continued or reinitiated. One recent study demonstrated, paradoxically, that a group of illicit opioid users who had "successfully" completed detoxification treatment were significantly more likely to die of drug overdose than those who had not completed the treatment.³² Other research has shown that unpredictable interactions between prescription and nonprescription drugs during treatment can lead to overdose risk. Such dynamics are particularly pertinent for the initiation phases of methadone treatment, during which disproportionately high rates of overdose have been reported because of opioid dosing dynamics and other (prescription or illicit) substance use.³³⁻³⁵ The rate of death due to overdose is greater during initial periods after release from prison,^{26,36} presumably because of an abrupt increase in drug consumption in conjunction with lowered tolerance. High depressive symptom scores have also been associated with overdose incidents.³⁷ Finally, a person who has experienced one overdose is at greater risk of another such incident.¹¹

Only in a minority of overdose incidents do drug users seek emergency assistance,^{6,9,11,38} largely because of fear of the consequences of revealing their illicit drug use or lack of confidence in the health care system.^{10,21} Increasing support is now being given to the concepts of providing training (e.g., in cardiopulmonary resuscitation) and resources (e.g., naloxone) to drug users as harm reduction strategies.^{9,39}

We undertook this study to examine the occurrence of and the factors associated with nonfatal overdose incidents in a cohort of illicit opioid users in 5 Canadian cities.

Methods

OPICAN is a project of the Interdisciplinary Health Research Team on Illicit Opiate Addiction Research, Treatment and Policy. This project is following a cohort of 679 regular illicit opioid users (i.e., people who use illicit opioids on most days each week for the past year) who were not enrolled in treatment at the time of recruitment. Subjects were recruited by a variety of methods, including dissemination of flyers at user contact points such as needle exchanges, advertisements in community papers and snowball sampling, between March and December 2002 in Vancouver, Edmonton, Toronto, Montréal and Québec. It is not possible to determine statistically defined representativeness in these samples because of the illegal nature of the participants' activities and the impossibility of probabilistic procedures for sampling from a known population (i.e., lack of a sampling frame listing all members of the target population).⁴⁰ However, care was taken to spread information about the study to a large variety of

drug user groups, peers and support contacts as suggested by a diverse pool of community liaisons in the local "drug scene" in each city. We are therefore confident that the sample obtained was as typical as possible.

The OPICAN study used a uniform screening and study protocol, and it received approval from a university or hospital ethics research board in each of the 5 cities. Subjects confirmed their eligibility through responses to a screening questionnaire, provided informed consent and were offered treatment, health and social service referrals if necessary. The study protocol consisted of an interviewer-administered questionnaire covering social, health and drug-use information; a depression assessment (Composite International Diagnostic Interview Short Form for Major Depression⁴¹); and an immunoassay antibody screening test of oral fluid for HIV, hepatitis C and hepatitis B. Assessments were performed on an anonymous basis (with each participant identified by a study code rather than by name), and all data were treated confidentially. Each subject received \$20 compensation for undergoing the assessment and all have been invited for follow-up assessments. For the analysis presented here, 28 cases were missing or excluded because of ambiguous responses; therefore, data for only 651 subjects were available for analysis.

The dependent variable in this study was self-reported overdose experience in the 6 months before assessment (referred to as an "overdose episode"). We defined an overdose experience as "a drug-use related experience where you lost consciousness and/or had convulsions because of too strong of a drug(s) or taking too much drug(s)." Bivariate analyses were performed, with the Pearson χ^2 statistic, to assess the association between overdose episodes and self-reported sociodemographic factors (age, sex, ethnicity, city and homelessness status) and 21 other factors covering personal and living situation, income, drug consumption (alcohol, heroin, cocaine, crack, hydromorphone, benzodiazepines or other opioids), injection drug use and frequency, physical and mental health, detention and use of health services. Route of drug administration was assessed for drugs for which more than 1 route of administration was common (hydromorphone, heroin and cocaine). The association between overdose episodes and age was assessed with a 2-sample *t* test. Marginally significant variables ($p < 0.10$) were examined with binary logistic regression to determine any independent effects and their respective odds ratios (ORs), with adjustment for sociodemographic factors.

Results

Key sociodemographic, drug-use and treatment characteristics of the OPICAN sample are presented in Table 1.

Overall, 112 (17.2%) of the 651 subjects reported an overdose episode in the previous 6 months; among these, 42/111 (37.8%) reported multiple episodes. In 63 cases (56.3%) the person was attended by ambulance personnel, and 50 (44.6%) received hospital attention during at least one of their recent overdose episodes. Almost one-quarter of the subjects (27 or 24.1%) did not receive any formal or informal assistance (Table 2).

Overdose episodes were not significantly associated with any of the sociodemographic variables ($p > 0.10$), except age (OR 0.97, 95% confidence interval [CI]

0.95–1.00) and homelessness (OR 1.86, 95% CI 1.12–3.10). Other predictors of overdose were consumption of alcohol (OR 1.69, 95% CI 1.07–2.67), consumption of benzodiazepines (OR 1.70, 95% CI 1.13–2.57), concurrent use of opioids and nonopioids (OR 1.68, 95% CI 1.03–2.73) and noninjection administration of hydromorphone in the past 30 days (OR 2.73, 95% CI 1.37–5.46). There were also associations with depression (OR 1.73, 95% CI 1.15–2.63), self-reported mental health problems (OR 1.51, 95% CI 0.99–2.30) and involvement in drug treatment in the past 12 months (OR 1.78, 95% CI 1.16–2.74).

When the factors identified as significant in the bivariate analyses were entered into a logistic regression analysis, homelessness, noninjection use of hydromorphone in the past 30 days and enrolment in drug treatment in the past 12 months emerged as significant predictors of overdose episodes ($p < 0.05$) (Table 3). Age was marginally significant (OR 0.98, 95% CI 0.95–1.00, $p = 0.082$).

The relations between overdose episodes and the 3 predictors of overdose identified by logistic regression analysis were examined with combined-sample data, an approach validated by the results of the Breslow–Day test of homogeneity of city-specific ORs ($p = 0.06$ for drug treatment, 0.68 for homelessness and 0.38 for noninjection use of hydromorphone). However, separate city-specific χ^2 analyses suggested that the overall significance of the associations of homelessness and noninjection use of hydromorphone with overdose episodes was largely driven by data from 2 cities: for homelessness, Vancouver (OR 2.42, 95% CI 1.02–5.75) and, to a lesser extent, Montréal (OR 3.26, 95% CI 1.26–8.43) (for the latter χ^2 analysis, 25% of cells had an expected count of less than 5); and for noninjection use of hydromorphone, Montréal only (OR 9.00, 95% CI 1.56–51.87). The significance of drug treatment was mostly attributable to data from Toronto (OR 3.26, 95% CI 1.28–8.33) and Québec (OR 5.10, 95% CI 1.52–17.12) (for the latter χ^2 analysis, 25% of cells had an expected count of less than 5).

Interpretation

In this study we examined the prevalence of and the factors associated with nonfatal overdose episodes among illicit opioid users from 5 Canadian cities who were not receiving treatment. Almost 1 in 5 subjects reported an overdose episode during the 6 months before assessment, and of those reporting such an episode, more than 1 in 3 had experienced multiple episodes. Overdose episodes were common within our sample, as has been documented for populations of illicit opioid users elsewhere.^{2–8}

Of every 5 subjects who reported an overdose episode, 2 had not received any kind of medical or emergency assistance. No association was found with sex, but age was inversely associated with occurrence of overdose. The latter finding, which is inconsistent with popular assumptions but which has been observed in other studies, suggests that such incidents are not more likely to occur among younger, less experienced drug users.^{5,11,42} However, we could not evaluate this finding further, because we had no information on duration of drug use.

After adjustment for sociodemographic and other variables, logistic regression analysis revealed 3 independent factors associated with overdose: homelessness, noninjection use of hydromorphone in the past 30 days and exposure to drug treatment in the past 12 months. The first of these associations is consistent with the literature,^{18,25,26} although in our study this result was driven primarily by the Vancouver subsample. Homelessness is a powerful social determinant of negative health status, and its association with poor health outcomes for drug users has been demonstrated previously.^{43,44}

The association with noninjection use of hydromorphone was mainly attributable to data from the Montréal sample. The literature suggests that the risk of overdose is higher with injection of opioids than with other administration routes.²⁸ However, further analyses revealed that this factor was significantly associated with benzodiazepine use ($r = 0.201$, $p = 0.003$), which itself demonstrated a bivariate association with

Table 1: Self-reported sociodemographic and drug use characteristics of illicit drug users in 5 Canadian cities

Characteristic	No. (and %) of subjects* <i>n</i> = 651	
Mean age (and SD), yr	34.8	(9.4)
No. of males	434	(66.7)
Ethnic background white	444	(68.2)
Living on the street	97	(14.9)
Use of nonopioid drugs† in past 30 d	616	(94.6)
Injection drug use in past 30 d	524	(80.5)
Drug treatment in past 12 mo	173	(26.6)

*Except where indicated otherwise.

†Nonopioid drugs consumed in the past 30 days: alcohol, benzodiazepines, cocaine, crack, speed, “downers” (e.g., secobarbital or phenobarbital).

Table 2: Overdose frequency and assistance received among illicit drug users in 5 Canadian cities

Characteristic	No. (and %) of subjects	
Overdose episodes in past 6 mo		
At least 1	112/651	(17.2)
More than 1*	42/111	(37.8)
Assistance received (<i>n</i> = 112)		
Assisted by ambulance personnel	63	(56.2)
Treated in hospital	50	(44.6)
Received naloxone	26	(23.2)
Assisted by friends only†	19	(17.0)
No assistance	27	(24.1)

*Percentage calculated with reference to the number of subjects who had at least 1 overdose. Data missing for 1 subject, so the denominator was 111.

†No medical assistance.

overdose. Therefore, noninjection use of hydromorphone may have served as a proxy for the concurrent use of benzodiazepines by subjects in our sample. The use of benzodiazepines (and other drugs) in conjunction with opioids is well documented as posing a greater risk for overdose.^{21,22,29,30,45,46}

Finally, subjects who had been exposed to drug treatment in the year before assessment were more likely to report an overdose episode. The most common treatment types were detoxification (62/172 or 36.0%) and clinic-based methadone maintenance (38/173 or 22.0%). Previous research has shown the potential antitherapeutic or iatrogenic effects of treatment for overdose;³¹ for example, treatment may lower users' drug tolerance⁵ or facilitate unfavourable pharmacodynamics between prescription and nonprescription drugs (e.g., concurrent use of methadone and benzodiazepines).

Our study had several limitations. The fact that we were unable to determine the representativeness of the sample clearly limits the generalizability of our results to other populations of drug users in and beyond the study sites. Furthermore, by using self-reported data we may have missed overdose experiences that had been forgotten, improperly recognized (positive or negative bias) or wilfully not reported. However, research on memory and self-reported data of even a sensitive nature (e.g., criminal activity or sex risks) among illicit drug users has shown that validity is high.^{47,48}

This study underlines the important role of housing — and social determinants in general — in determining the health of marginalized populations. Housing and other forms of social support may help to reduce health risks for illicit

drug users, including the risk of overdose. The demonstrated association of overdose episodes with use of multiple drugs requires further investigation. Clearly, measures are needed to increase awareness among users and care providers about the risks associated with consumption of both prescription and illicit substances. Further efforts are needed to untangle the complex dynamics of the potential antitherapeutic effects of treatment, as suggested by our data. Such efforts must take into account the fact that many treatment episodes for illicit drug users are suddenly or prematurely terminated, which leaves no opportunity for transition measures.

Further study is also needed to determine why so few subjects used emergency services for overdose episodes. Systematic provision to drug users of overdose resources and response training — including naloxone and training in cardiopulmonary resuscitation^{9,39} — may be one way to address these response gaps.

Our results suggest that a complex combination of factors is associated with overdose episodes among the illicit opioid users in the OPICAN study. Interventions are more likely to be effective if they can be directed to some of these specific causal factors.

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Table 3: Variables associated with drug overdose within the past 6 months*

Variable†	No. of subjects	No. (and %) with overdose	OR (and 95% CI)	
			Crude	Adjusted‡
Social, health and treatment characteristics				
Living on the street	97	25 (25.8)	1.86 (1.12–3.10)	1.96 (1.10–3.48)
Depression§	322	68 (21.1)	1.73 (1.15–2.63)	1.26 (0.78–2.01)
Mental health problem	211	45 (21.3)	1.51 (0.99–2.30)	1.17 (0.71–1.91)
Drug treatment in past 12 mo	173	41 (23.7)	1.78 (1.16–2.74)	1.70 (1.05–2.75)
Drugs consumed¶				
Alcohol	422	83 (19.7)	1.69 (1.07–2.67)	1.44 (0.88–2.37)
Benzodiazepines	234	52 (22.2)	1.70 (1.13–2.57)	1.36 (0.83–2.23)
Opioids in combination with nonopioids	458	88 (19.2)	1.68 (1.03–2.73)	1.63 (0.97–2.73)
Hydromorphone route of administration				
No consumption (reference)	434	69 (15.9)	1.00	1.00
Injection	155	23 (14.8)	0.92 (0.55–1.54)	0.87 (0.46–1.64)
Oral, nasal, smoked	62	20 (32.2)	2.52 (1.40–4.55)	2.37 (1.20–4.71)

Note: OR = odds ratio, CI = confidence interval.

*Variables were identified by bivariate analysis and were then subjected to logistic regression.

†Self-reported, except for depression.

‡The fully adjusted model included all variables shown in this table, as well as age, sex, ethnicity and city.

§Based on Composite International Diagnostic Interview Short Form for Major Depression.⁴¹

¶In past 30 days.

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