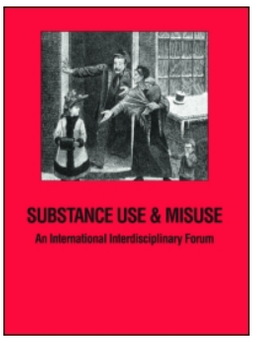

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Factors Associated with Nonfatal Overdose During a Public Health Emergency

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ABSTRACT

Background: In 2016, in the Canadian province of British Columbia, the Provincial Health Officer declared drug-related overdose deaths a public health emergency. *Objectives*: In this study, we examine factors associated with recent non-fatal overdose during a time of unprecedented rates of overdose and increasing involvement of fentanyl and fentanyl derivatives in overdose deaths. *Methods*: Between June and September 2016, a cross-sectional survey was conducted among people who inject drugs (PWID) in Victoria, British Columbia, Canada. Bivariable and multivariable logistic regression analyses were used to examine factors associated with recent non-fatal overdose. *Results*: A total of 187 PWID were included in the present study, of whom 56 (29.9%) reported having overdosed in the previous 6 months. In multivariable analyses, fentanyl injection (Adjusted Odds Ratio [AOR] = 2.60; 95% confidence interval [CI]: (1.08 – 6.27) and public injection (AOR = 2.20; 95% CI: 1.09 – 4.43) were positively associated with recent non-fatal overdose. *Conclusions*: Fentanyl injection and public injection were associated with an increased likelihood of non-fatal overdose. These findings underscore the need for drug checking, safer sources of opioids and safer injecting interventions as part of overdose prevention strategies.

KEYWORDS
Fentanyl; illicit drugs; injection drug users; nonfatal overdose

Introduction

Canada, like many areas in the United States, is experiencing unprecedented rates of overdose deaths. In 2016, in the Canadian province of British Columbia (B.C.), the Provincial Health Officer declared drug-related overdoses a public health emergency (BC Health, 2016). The B.C. coroner's office reported over 1,400 apparent illicit drug overdose deaths in 2017, an estimated 177% increase from 2015 (BC Coroners Service, 2018). At 30 deaths per 100,000 individuals, the rate of illicit drug overdose deaths in the province is now dramatically higher than just 6 years earlier when 5 illicit drug overdose deaths per 100,000 was the norm then and in the previous decade (BC Coroners Service, 2018).

Toxicology tests detected illegal fentanyl in 83% of overdose fatalities in B.C. in 2017 (BCCDC, 2018). Such illicit fentanyl–detected deaths appear to account largely for the increase in illicit drug overdose deaths in the province over the previous 5 years, as the number of illicit drug overdose deaths excluding fentanyl remained relatively stable during this time period (BC Coroners Service, 2018). Fentanyl and fentanyl derivatives have also been recognized in other jurisdictions as increasingly present in the illicit drug markets (Carroll, Marshall, Rich, & Green, 2017; Ciccarone, 2017; Kerensky & Walley, 2017).

In the midst of alarming rates of fatal overdoses, many more individuals are experiencing non-fatal overdoses and interventions, such as naloxone administration, have played a critical role in the response to fentanyl-related overdoses (Kerensky & Walley, 2017). In declaring the public health emergency in B.C, officials highlighted the inadequate reporting of nonfatal overdose incidents, including those at which naloxone had been administered. A stated objective, in the declaration of a public health emergency, was to enable more information gathering on the context of non-fatal overdose incidents in order to help target action and better protect people

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who use drugs (BC Health, 2016). We therefore undertook the present study to examine the prevalence of and factors associated with recent non-fatal overdose among people who inject drugs (PWID) in Victoria, B.C., a medium-sized Canadian city with an estimated 3000 individuals injecting drugs (van Dam-Bates, Fyfe, & Cowen, 2015), often within high risk environments, including public settings (Ivsins et al., 2012; MacNeil & Pauly, 2010). Understanding the risk factors associated with non-fatal overdose among PWID in this setting during a time of unprecedented rates of overdose driven by fentanyl and fentanyl derivatives may help inform interventions to address the current public health emergency.

Methods

Six months into the declared public health emergency, a cross-sectional study of people who inject drugs (PWID) was conducted to investigate the feasibility of supervised consumption services in Victoria. Between June and September 2016, PWID were recruited through convenience sampling at sites distributing clean injecting supplies. Eligibility criteria included being age eighteen or older and having injected illicit drugs in the previous 6 months. Participants completed an interviewer-administered questionnaire that elicited information regarding sociodemographic characteristics, drug use behaviors, health and social service utilization, as well as willingness to use and design and programmatic preferences for supervised consumption services. All participants provided written informed consent and were provided with a $20 CAD honourarium. The study had ethical approval from the University of Victoria Research Ethics Board.

The primary outcome variable examined for this analysis was recent non-fatal overdose, defined in response to the question, "Have you overdosed in the past 6 months?" (yes vs. no). Prior to asking this question, interviewers read aloud the following preamble to participants: "For this study, an overdose means having too much of a drug (or combination of drugs) for your body to be able to cope with. There are a number of signs or symptoms that show someone has overdosed, and these differ with the type of drug used…" Interviewers then described common respective signs of depressant drug overdose (shallow breathing or not breathing at all; snoring or gurgling sounds; blue lips or fingertips; floppy arms and legs; no response to stimulus; disorientation; unarousable [i.e., can't be woken up]; unconsciousness) and stimulant drug overdose (chest pain; disorientation/confusion; severe headache; seizures; high temperature; difficulty breathing; agitation and paranoia; hallucination; unconsciousness).

We selected social, demographic, and behavioral variables to be considered as explanatory variables on the basis of previous research investigating overdose among PWID (Bohnert, Tracy, & Galea, 2009; Coffin et al., 2007; Darke & Farrell, 2014; Escudero et al., 2016; Holloway, Bennett, & Hills, 2016; Horyniak et al., 2013; Kerr et al., 2007; Lake et al., 2015) and *a priori* hypothesized relationships. Survey variables considered included: age (per year older); current gender identity (women vs. men); ancestry (White vs. non-White); injection heroin use (≥daily vs. <daily); injection crystal methamphetamine use (≥daily vs. <daily); injection cocaine use (≥daily vs. <daily); injection fentanyl use (≥daily vs. <daily); smoke crack cocaine or crystal methamphetamine (≥daily vs. <daily); heavy alcohol use (yes vs. no); public injection (always or usually vs. sometimes, occasionally or never); inject alone (always or usually vs. sometimes, occasionally or never); require help injecting (always or usually vs. sometimes, occasionally or never); homelessness (yes vs. no); incarceration (yes vs. no); participation in residential addiction treatment (yes vs. no); and frequency of reading public health drug alerts (all or most of the time vs. some or none of the time). In accordance with recommendations by the National Institutes on Alcohol Abuse and Alcoholism (NIAAA) (Moyer, 2013), heavy alcohol use was defined in response to the single-item screening question, "How often in the past 12 months have you had [5 for men/4 for women] or more drinks on one occasion?" (≥weekly = yes; <weekly = no). Frequency of reading public health drug alerts was defined in response to the question, "In the past 12 months, how often have you read public advisories warning of drug risks and overdoses?" All other variables refer to the 6 months preceding the interview date unless otherwise indicated.

Bivariable statistics were used to determine factors associated with nonfatal overdose. Categorical explanatory variables were analyzed using Pearson's χ^2 test or Fisher's exact test when one or more cells contained expected values less than or equal to five. Continuous variables were analyzed using the Mann-Whitney U test. Unadjusted odds ratios were calculated using bivariable logistic regression. We then applied an *a priori*-defined statistical protocol to construct an explanatory multivariable logistic regression model. First, we constructed a full model including

explanatory variables that were significant at the level of $p \leq .20$ in bivariable analyses. This set of variables was then subjected to a backward selection procedure based on the Akaike information criterion (AIC) and Type III p values (Lima et al., 2008). Each variable with the highest p value was removed sequentially, with the final model including the set of variables associated with the lowest AIC. This procedure balances model selection on finding the best explanatory model with best model fit (Lima et al., 2008).

Finally, we produced descriptive statistics to examine the circumstances of most recent overdose event among those who reported having overdosed in the previous 6 months. Specifically, responses to the following questions were analyzed: "The last time you overdosed, which injection or non-injection drugs or substances did you take?" and "Could you tell me the specific place [where you last overdosed]?" Participants could provide more than one response to the question regarding substance(s) used. Responses regarding overdose location were allocated into the following mutually exclusive categories: indoor housing; indoors at an organization or shelter; outdoors/on the street; public space other than outdoors. In

Table 1. Bivariable analyses of factors associated with recent non-fatal overdose[a] among 187 people who inject drugs in Victoria, British Columbia, Canada (2016).

Characteristic	Non-fatal overdose[a] Yes; *n* (%) 56 (29.9%)	Non-fatal overdose[a] No; *n* (%) 131 (70.1%)	Odds ratio (95% CI)	*p* value
Age				
Median (IQR[b])	35.0 (28.3 – 43.7)	42.0 (33.1 – 50.0)	0.95 (0.93 – 0.98)	.003
Gender				
Women	18 (32.1)	48 (36.6)	0.82 (0.42 – 1.59)	.556
Men	38 (67.9)	83 (63.4)		
Ancestry				
White	35 (62.5)	81 (61.8)	1.03 (0.54 – 1.96)	.931
Non-White	21 (37.5)	50 (38.2)		
Heroin injection[a]				
≥Daily	33 (58.9)	42 (32.1)	3.04 (1.59 – 5.80)	.001
<Daily	23 (41.1)	89 (67.9)		
Crystal methamphetamine injection*				
≥Daily	26 (46.4)	30 (22.9)	2.92 (1.50 – 5.67)	.002
<Daily	30 (53.6)	101 (77.1)		
Cocaine injection[a]				
≥Daily	1 (1.8)	2 (1.5)	1.17 (0.10 – 13.20)	1.000
<Daily	55 (98.2)	129 (98.5)		
Fentanyl injection[a]				
≥Daily	18 (32.1)	13 (9.9)	4.30 (1.93 – 9.58)	<.001
<Daily	38 (67.9)	118 (90.1)		
Smoke crack cocaine or crystal methamphetamine[a]				
≥Daily	12 (21.4)	26 (19.8)	1.10 (0.51 – 2.38)	.806
<Daily	44 (78.6)	105 (80.2)		
Heavy alcohol use[c]				
Yes	11 (19.6)	31 (23.7)	0.79 (0.59 – 1.69)	.547
No	45 (80.4)	100 (76.3)		
Public injection[a]				
Always or usually	32 (57.1)	39 (29.8)	3.15 (1.65 – 6.02)	.001
Sometimes, occasionally or never	24 (42.9)	92 (70.2)		
Inject alone[a]				
Always or usually	22 (39.3)	53 (40.5)	0.95 (0.50 – 1.81)	.881
Sometimes, occasionally or never	34 (60.7)	78 (59.5)		
Require help injecting[a]				
Always or usually	6 (10.7)	16 (12.2)	0.86 (0.32 – 2.33)	.771
Sometimes, occasionally or never	50 (89.3)	115 (87.8)		
Homeless[a]				
Yes	37 (66.1)	54 (41.2)	2.78 (1.45 – 5.34)	.002
No	19 (33.9)	77 (58.8)		
Incarcerated[a]				
Yes	16 (28.6)	23 (18.0)	1.88 (0.90 – 3.91)	.092
No	40 (71.4)	108 (82.0)		
Participation in residential addiction treatment[a]				
Yes	6 (10.7)	12 (9.2)	1.19 (0.42 – 3.35)	.789
No	50 (89.3)	119 (90.8)		
Reads public health drug alerts[c]				
All or most of the time	33 (58.9)	82 (62.6)	0.86 (0.45 – 1.63)	.637
Some or none of the time	23 (41.1)	49 (37.4)		

[a]Refers to previous 6 months.
[b]IQR = interquartile range.
[c]Refers to previous 12 months.

addition, we examined responses to questions about whether or not participants were with other people, an ambulance was called, or they were administered Narcan/naloxone when they most recently overdosed (all yes vs. no). Finally, we descriptively examined the proportion of these participants who used heroin or fentanyl, respectively, in the previous 6 months (≥daily, at least once but < daily vs. never). All statistical analyses were performed using IBM SPSS Statistics software version 23.0. All p values are two-sided.

Results

A total 187 PWID were eligible and included in the present study. Of these, 66 (35.3%) were women, 116 (62.0%) were Caucasian and the median age was 40.0 (interquartile range [IQR] = 32.0 – 49.0). In total, 56 participants (29.9%) reported having overdosed at least once in the previous 6 months. Of these 56 participants, 18 (32.1%) were women, 35 (62%) were Caucasian and the median age was 35.0 (IQR = 28.3 – 43.7).

The results of the bivariable analyses are shown in Table 1. Factors that were significantly and positively associated with recent nonfatal overdose in bivariable analyses included: heroin injection (odds ratio [OR] = 3.04; 95% confidence interval [CI] = 1.59 – 5.80); crystal methamphetamine injection (OR = 2.92; 95% CI = 1.50 – 5.67); fentanyl injection (OR = 4.30; 95% CI = 1.93 – 9.58); public injection (OR = 3.15; 95% CI = 1.65 – 6.02); and homelessness (OR = 2.78; 95% CI = 1.45 – 5.34). Age was significantly and negatively associated with the outcome (OR = 0.95; 95% CI = 0.93 – 0.98) in unadjusted analyses.

As shown in Table 2, in multivariable analyses, factors that remained significantly and positively associated with recent non-fatal overdose included: fentanyl injection (adjusted odds ratio [AOR] = 2.60; 95% CI = 1.08 – 6.27) and public injection (AOR = 2.20; 95% CI = 1.09 – 4.43).

Table 2. Multivariable logistic regression analyses of factors associated with recent nonfatal overdosea among 187 people who inject drugs in Victoria, British Columbia, Canada (2016).

Variable	Adjusted odds ratio (AOR)	95% confidence interval (CI)	p value
Heroin injection[a] (≥daily vs. <daily)	1.89	(0.92 – 3.88)	.085
Crystal methamphetamine injection[a] (≥daily vs. <daily)	2.03	(0.98 – 4.17)	.056
Fentanyl injection[a] (≥daily vs. <daily)	2.60	(1.08 – 6.27)	.033
Public injection[a] (always or usually vs. sometimes, occasionally or never)	2.20	(1.09 – 4.43)	.027

[a]Refers to previous 6 months.

Among the 56 participants who had overdosed in the previous 6 months, the most commonly reported substances used at their most recent overdose event were: heroin (n = 47; 83.9%); fentanyl (n = 23; 41.1%); and crystal methamphetamine or amphetamines (n = 16; 28.6%). With regards to location of most recent overdose, 21 (37.5%) participants reported having overdosed outdoors/on the street; 16 (28.6%) at an organization or shelter; 15 (26.8%) in indoor housing; and 4 (7.1%) in a public space other than outdoors (e.g., public washroom, abandoned building). A total of 42 participants (75.0%) reported that they were with other people when they most recently overdosed; 40 (71.4%) reported that an ambulance was called, and 39 (69.6%) reported having been administered Narcan/naloxone at their most recent overdose event. In total, 33 of the 56 participants (58.9%) reported ≥ daily heroin use and 21 (37.5%) reported using heroin at least once but < daily in the previous 6 months. Seventeen participants (30.4%) reported ≥ daily fentanyl use and 26 (46.4%) reported using fentanyl at least once but < daily in the previous 6 months.

Discussion

This survey of PWID in a medium-sized Canadian city reports on recent non-fatal overdose experiences during a time when authorities declared a public health emergency in response to increasing illicit overdose deaths. Nonfatal overdose was common, with a third reporting having overdosed at least once in the last 6 months. Factors associated with recent non-fatal overdose in adjusted analyses included injecting fentanyl (knowingly or suspected) and public injection. Almost half of those who had recently overdosed reported that their most recent overdose event occurred outdoors or in a public space, just over a quarter reported that they had overdosed in a service organization or shelter and another quarter reported having overdosed in indoor housing. Participants most commonly reported use of heroin and/or fentanyl at their most recent overdose event. The majority of participants reported being with other people and having been administered naloxone as well as having an ambulance respond to the overdose event.

Our study found a high prevalence of reported nonfatal overdose in the previous 6 months among

PWID during a time when fatal overdoses were being recorded at unprecedented rates. This is an obvious concern due to the potential detrimental health impacts of non-fatal overdose on the person, including hypoxic brain injury, aspiration pneumonia, peripheral neuropathy, seizures and renal failure (Warner-Smith, Darke, & Day, 2002). While those who have died of overdose may differ from our sample, non-fatal overdose has been found to increase the risk of a subsequent fatal overdose (Caudarella et al., 2016; Coffin et al., 2007; Stoové, Dietze, & Jolley, 2009). Overdose events are also a significant traumatic event for those present at the occurrence, notably those responding, which often includes nontraditional first-responders such as other people who use drugs, shelter and harm reduction workers and others (Holloway et al., 2016; Wallace et al., 2016).

Understanding the factors that may contribute to risk of nonfatal overdose during an overdose crisis is critical to inform interventions. Despite existing research, there continues to be questions related to risk factors that may predict nonfatal overdose and data addressing such questions could inform policy and programmatic interventions (Escudero et al., 2016), particularly when the drug supply is evolving as it is currently in much of North America (Fairbairn, Coffin, & Walley, 2017; Frank & Pollack, 2017; Gladden, Martinez, & Seth, 2016). Much of the existing research on correlates of non-fatal overdose among PWID has focused on heroin-related overdose. Prior to the introduction of fentanyl in the illicit drug market, frequent heroin use was confirmed as a common risk factor for overdose for a similar population of PWID in Vancouver, B.C (Kerr et al., 2007). Fentanyl derivatives are now increasingly sold as heroin and replacing heroin (Misailidi et al., 2017).

The findings from our study provide recognition of the existence of fentanyl injection as significantly associated with an increased likelihood of non-fatal overdose. Whereas fentanyl has previously been considered "low use but high risk/harm" substance' in some contexts (Mounteney, Giraudon, Denissov, & Griffiths, 2015), the overdose emergency in this Canadian province indicates that fentanyl and its analogs are pervasive and create significant risks among people who use illicit drugs (BCCDC, 2017). Fentanyl and fentanyl derivatives are increasingly found to be within a range of illicit drugs and not solely opioids such as heroin but also stimulants (Lysyshyn, 2017). The arrival of fentanyl has arguably changed the definition of drugs themselves and the concept of contaminants (Ciccarone, Ondocsin, & Mars, 2017). These findings point to the need for the further development and evaluation of drug checking within harm reduction responses as a possible measure to identify and potentially reduce the use of adulterated drugs among PWID. Further, the scale-up of legally prescribed opioid substitution treatment programs, including injectable diacetylmorphine and hydromorphone, may also help to mitigate fatal and non-fatal overdose among this population (Oviedo-Joekes et al., 2016). With the implementation of such programs being limited and cumbersome to date there have also been appeals for legal regulation of all criminalized drugs (Boyd, Murray, & MacPherson, 2017).

The study data are from a sample that includes a high proportion of people experiencing homelessness, who frequently inject in public, which was found to be significantly associated with an increased likelihood of experiencing nonfatal overdose. This finding is consistent with previous research in which injecting in public and vulnerabilities related to poverty and homelessness were associated with non-fatal overdose (Kerr et al., 2007; Pauly, Wallace, & Barber, 2018). The high prevalence of public injection among PWID experiencing non-fatal overdose and our descriptive findings demonstrating that almost half of recent overdose events occurred in public spaces point to the need to include housing and responses to homelessness as part of harm reduction strategies (DeBeck et al., 2009). Further, these findings underscore the need to remove governmental barriers in order to allow for the rapid scaling-up of supervised consumption services, which have been shown to effectively address risks of overdose and related harms among structurally vulnerable PWID, including those who would otherwise inject in public settings (Marshall, Milloy, Wood, Montaner, & Kerr, 2011; Small, Rhodes, Wood, & Kerr, 2007). Prior research has documented how it is those individuals experiencing homelessness in which public injecting is common who often access supervised consumption facilities when established (Wood et al., 2005).

We also found that over a quarter of recent nonfatal overdose incidents were reported by participants to have taken place within a homeless shelter or nongovernmental organization (NGO). These findings resemble results from a 2013 survey in Wales that found overdose events were frequently occurring within homeless shelters (hostels). It was in these sites where overdoses were first being responded to with naloxone and often by those at the site and not

necessarily ambulance and paramedics (Holloway et al., 2016). Our study found naloxone was administered at 70% of nonfatal overdose events. Previous research by the authors has documented the high frequency of overdose events at homeless shelters as well as NGO washrooms requiring staff to respond with administration of naloxone, often resulting in traumatic impacts on staff (Wallace et al., 2016). Together these findings highlight the importance of providing housing and safer injecting interventions as well as adequate training and support for staff, family and friends as part of the scale up and wide spread distribution of naloxone.

This study has several limitations. First, this study relied on cross-sectional data and we were therefore unable to draw conclusions regarding the temporal nature of the associations observed herein. Second, the study used convenience sampling within the locations that included the primary and secondary needle exchange services and may underrepresent those who do not access inner-city health and social services. Third, nonfatal overdose and all other variables are self-reported and therefore subject to potential biases and inaccuracies, including social desirability bias and deficiencies in recall. Fourth, due to low cell counts, we were underpowered to examine the association between various levels of drug use intensity and likelihood of nonfatal overdose. We were also underpowered to characterize factors associated with receiving naloxone or medical attention in the event of overdose. Future studies should seek to address these knowledge gaps in effort to provide information to guide the development and implementation of interventions to mitigate overdose and related harms.

In summary, we found that nonfatal overdose was common among this sample of PWID, with a third of participants reporting experiencing a recent nonfatal overdose event during a time of unprecedented overdose rates in this setting. Fentanyl injection and public injection were associated with an increased likelihood of experiencing nonfatal overdose. These findings may help to inform interventions to address current overdose crises and in particular underscore the importance of offering drug checking, safer sources of opioids, including injectable opioid treatments, and safer injecting interventions as potential measures to reduce overdose and related harms among PWID.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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