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## The relationship between parental heavy drinking and non-fatal overdose among people who inject drugs in Vancouver, Canada

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### Abstract

**Background:** Despite the acute drug-related and behavioural risk factors for experiencing a drug overdose, few remote childhood experiences have been examined as risk factors for subsequent later life overdose risk. Parental heavy drinking has been associated with some later life negative outcomes, but little is known regarding the impact on drug overdoses, especially among people who inject drugs. Given the current overdose crisis in North America, we sought to evaluate the impact of parental heavy drinking on later life non-fatal overdose among people who inject drugs in Vancouver, Canada.

**Methods:** Data were derived from two prospective cohort studies of community-recruited people who inject drugs in Vancouver between December 2012 and May 2016. We employed multivariable generalized estimating equations to examine the relationship between parental heavy drinking and non-fatal overdose in the past six months.

**Results:** Among 327 eligible participants, 111 (33.9%) reported parental heavy drinking and 95 (29.1%) reported a non-fatal overdose at least once during the study period. In a multivariable analysis, experiencing parental heavy drinking remained independently associated with non-fatal overdose (adjusted odds ratio: 1.69; 95% confidence interval: 1.07–2.66) after adjustment for a range of socio-demographic and drug using confounders.

**Conclusions:** These findings suggest long-term negative impacts of parental heavy drinking, on subsequent risk taking or other mechanisms associated with overdose. Current overdose

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#### CONFLICT OF INTEREST

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prevention efforts may benefit from the evaluation of life course vulnerabilities that may be amenable to earlier interventions.

### Keywords

Childhood exposures; overdose; morbidity; alcohol; parental heavy drinking

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## 1. INTRODUCTION

Among people who use illicit drugs, acute toxicity (overdose) remains the most common cause of premature mortality (Davis, Suleta, Corsi, & Booth, 2017), with rates even higher for those who inject drugs (Mathers et al., 2013). Further, a variety of long-term health conditions result as a consequence of non-fatal overdoses including pulmonary complications, muscular complications, renal failure, cardiovascular complications, and cognitive impairment (Warner-Smith, Darke, & Day, 2002). Perhaps the most concerning aspect of experiencing a non-fatal overdose is the increased risk of a subsequent fatal overdose (Caudarella et al., 2016). A recent systematic review estimated the worldwide lifetime prevalence of experiencing an unintentional drug overdose to be 45% among illicit drug using populations (Martins, Sampson, Cerda, & Galea, 2015). However, in recent years communities across North America have been experiencing devastating rates of drug overdoses partially due to the contamination of illicit drug supply (particularly the heroin supply) by illicit fentanyl (Hedegaard, Warner, & Minino, 2017; Somerville et al., 2017). To combat the ongoing overdose epidemic determining exposures associated with an increased risk of overdose are essential to design effective interventions for people at high-risk.

Childhood represents a period of critical development where adverse family environments have been shown to impact brain development, emotional regulation, and increase psychological distress through various pathways, resulting in poor health outcomes (Yap, Allen, & Ladouceur, 2008; Yap, Whittle, et al., 2008). While heavy alcohol drinking is a significant contributor to mortality and morbidity worldwide, with an estimated 18.9% of Canadians aged 12 and older reported heavy drinking, there is a dearth of research examining the impact of growing up with a parent who drank heavily (Rehm et al., 2009; Rehm et al., 2003; Statistics Canada, 2013). The limited research investigating parental heavy drinking has primarily focused on alcohol outcomes and identified associations ranging from earlier initiation into alcohol consumption to increased alcohol dependence in adulthood (Parker & Harford, 1987; Rossow, Keating, Felix, & McCambridge, 2016). For many individuals, heavy drinking is indicative of alcohol misuse (Lloyd & Kepple, 2017). While the concurrent use of opioids and alcohol is an established risk factor for drug overdose (Shah, Lathrop, Reichard, & Landen, 2008), previous research has also indicated that many other potential pathways might exist linking parental heavy drinking with adult non-fatal drug overdoses, including factors such as depressive symptoms, low social support, juvenile delinquency, dysfunctional family environments, and low family cohesion (Bijttebier & Goethals, 2006; Finan, Schulz, Gordon, & Ohannessian, 2015; Pabayo, Alcantara, Kawachi, Wood, & Kerr, 2013; Snyder & Merritt, 2015).

Given the well-researched consequences associated with non-fatal overdose, conducting research identifying childhood exposures known to increase overdose risk is essential to design effective prevention strategies. Few research studies have investigated drug overdoses associated with growing up with a heavy drinking parent. To our knowledge, no studies have focused on populations of people who inject drugs. As people who inject drugs are known to experience the highest rates of non-fatal overdoses among people who use drugs, this is an important sub-population to focus on (Mathers et al., 2013). Drawing on data from two long-running prospective cohorts of people who use drugs in Vancouver, we sought to determine if experiencing parental heavy drinking during childhood was associated with an increased risk of non-fatal overdose among people who inject drugs in this setting.

## 2. METHODS

### 2.1 Study Procedures

The Vancouver Injection Drug Users Study (VIDUS) and the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS) are ongoing open prospective cohorts of adult drug users recruited through word of mouth, street outreach, and referrals from community organizations in Vancouver, Canada. These studies have been described in detail previously (Strathdee et al., 1998; Tyndall et al., 2003; Wood et al., 2004). Briefly, VIDUS enrolls HIV-negative persons who reported injecting an illicit drug at least once in the month preceding enrollment; ACCESS enrolls HIV-positive individuals who report using an illicit drug (other than, or in addition to, cannabis) in the previous month. For both cohorts, other eligibility criteria included being aged 18 years or older, residing in the greater Vancouver region and providing written informed consent. The study instruments and all other follow-up procedures for each study are harmonized to permit combined analyses. At baseline and semi-annually thereafter, participants complete an interviewer-administered questionnaire eliciting socio-demographic data as well as information pertaining to drug use patterns, risk behaviors, and health care utilization. Nurses collect blood samples for HIV and hepatitis C virus serology, provide basic medical care, and arrange referrals to appropriate health care services if required. Participants receive a \$40 (CDN) honorarium for each study visit. The University of British Columbia/Providence Health Care Research Ethics Board provided ethical approval for both studies. The study setting of Vancouver includes the Downtown Eastside (DTES) which is home to a large open drug scene (Wood & Kerr, 2006), with a range of harm reduction programs and treatments for drug use disorders including Insite, North America's first supervised injection facility (Marsh & Fair, 2006).

All participants who completed the baseline questionnaire between December 1, 2012 and May 31, 2016, were included in the present analysis. Additionally, at each follow-up, the sample was restricted to individuals who reported injection drug use in the previous six months. In total seven waves of data collection were included in the present analysis.

### 2.2 Study Variables

The primary outcome of interest was non-fatal overdose in the previous six months. This was defined as responding "yes" to the question: "In the last six months, have you overdosed by accident (i.e., where you had a negative reaction from using too much drugs or had a bad

trip)?” Our definition of non-fatal overdose using a self-reported measure is consistent with previous research, including those from the VIDUS/ACCESS cohort and others (Hunter et al., 2018; Lake et al., 2015).

The primary explanatory variable of interest was parental heavy drinking while growing up. This was defined as reporting “mother”, “father”, “adoptive parent”, “foster parent”, “stepmother”, or “stepfather” to the question “Who did you live with most between birth and age 16?” and subsequently reporting “drank heavily” for those individuals, to the question: “Did they drink heavily? By ‘drink heavily’, I mean on average more than 4 drinks a day for a woman, or more than 5 drinks a day for a man.” Our definition of heavy drinking is consistent with the Canadian Government’s definition (Statistics Canada, 2013).

We also considered secondary explanatory variables that might confound the relationship between parental heavy drinking and non-fatal overdose. These included socio-demographic characteristics, including: age (per year older); sex (female vs. male); ancestry (white vs. non-white); homelessness in the previous six months, defined as having no fixed address, sleeping on the street, or staying in a shelter or hostel (yes vs. no); and residing in the DTES in the previous six months (yes vs. no). Drug-use variables referred to behaviours in the previous six months, and included: daily injection heroin use (yes vs. no) and daily injection stimulant use (specifically powder or crack cocaine or crystal methamphetamine) (yes vs. no). Other exposures and health status included: incarceration in the previous six months (yes vs. no); engagement in opioid agonist therapy (yes vs. no); and HIV serostatus (positive vs. negative).

### 2.3 Statistical Analysis

As a first step, we examined the baseline sample characteristics stratified by non-fatal overdose, using the Pearson’s Chi-squared test (for binary variables) and Wilcoxon Rank Sum test (for continuous variables). Fisher’s exact test was used when one or more of the cells contained expected values less than or equal to five.

Since the analyses of non-fatal overdose included serial measures for each participant, we used generalized estimating equations (GEE) with logit link, which provided standard errors adjusted by multiple observations per person using an exchangeable correlation structure. All missing data was removed from the analysis. We first used bivariable GEE analyses to examine the association between each explanatory variable and non-fatal overdose. To examine the relationship between parental heavy drinking and non-fatal overdose, we fit multivariable GEE models using a conservative confounding model selection approach (Ti et al., 2012). We included all variables that were associated with non-fatal overdose in unadjusted analyses, and used a stepwise approach to fit a series of reduced models. After comparing the value of the coefficient of parental heavy drinking in each reduced model, we dropped the secondary variable associated with the smallest relative change. We continued this iterative process until the minimum change exceeded 5 %. In order to examine whether participants with fewer data points were meaningfully different from those with more data, we also conducted a sensitivity analysis where we repeated the baseline analysis stratified by those who completed only one interview and those with multiple interviews completed. All *p*-values are two sided and tests were considered statistically significant at  $p \leq 0.05$ . All

statistical analyses were performed using R software version 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria [2016]).

### 3. RESULTS

In total, 327 participants were eligible for the present study, with 181 (55.4%) from VIDUS and 146 (44.6%) from ACCESS. Among this sample, 147 (45.0%) were women and the median age at baseline was 36.2 years (interquartile range [IQR] = 31.0–45.2). The self-reported ethnicity of the participants were 163 (49.8%) white ancestry, 131 (40.1%) First Nations/Aboriginal/Inuit/Metis, 24 (7.3%) South Asian/Latin American, 7 (2.1%) Black, and 2 (0.6%) Chinese/other Asian. Overall, the 327 individuals contributed 929 observations to the analysis and the median number of follow-up visits was 2 (IQR: 1–4) per person. The baseline characteristics of all participants stratified by non-fatal overdose are presented in Table 1. As shown at baseline each of those who were younger, reported parental heavy drinking, were homeless, resided in the DTES, injected heroin daily, injected stimulants daily, were incarcerated, and were HIV positive were more likely to have experienced a non-fatal overdose in the previous six months (all  $p < 0.05$ ). Additionally, among the 327 individuals included in the study 111 (33.9%) reported parental heavy drinking and 95 (29.1%) reported a non-fatal overdose at least once during the study period. Throughout the study period a total of 21 participants (6.4%) were lost to follow-up, defined as participants not interviewed for at least three years.

The results of the bivariable and multivariable GEE analyses of non-fatal overdose are presented in Table 2. As shown, in the final multivariable model after adjusting for a range of potential confounders, participants who reported experiencing parental heavy drinking in childhood had an increased odds of non-fatal overdose (adjusted odds ratio [AOR] = 1.69; 95% confidence interval [CI]: 1.07–2.66). Further, homelessness (AOR = 2.20; 95% CI: 1.41–3.44) and HIV serostatus (AOR = 0.40; 95% CI: 0.25–0.63) were identified as significant confounders in this model.

The sensitivity analysis included all 327 study participants with 102 (31.2%) having only one interview completed and 225 (68.8%) with multiple interviews. Two variables were significantly different between the two groups at baseline: the proportion reporting homelessness was higher among those completing only one interview compared to those with multiple interviews (55.9% vs. 37.8%,  $p = 0.002$ ), but the proportion reporting childhood emotional abuse was lower among this group (31.4% vs. 44.4%,  $p = 0.017$ ). There was no significant difference in reporting the primary outcome (16.7% vs. 12.9%,  $p = 0.371$ ) or primary explanatory variable (35.3% vs. 33.3%,  $p = 0.729$ ) between the two groups.

### 4. DISCUSSION

We observed high rates of reported parental heavy drinking among our sample of people who inject drugs in Vancouver, Canada, with approximately one-third of participants reporting the exposure. In the multivariable analysis, parental heavy drinking was significantly and positively associated with recent non-fatal overdose. Homelessness and

HIV serostatus were identified as significant confounders, consistent with previous research findings (Walley et al., 2014; Winter et al., 2015).

Our findings that those with a parent who was a heavy drinker were more likely to report a non-fatal overdose has not been previously reported, but previous studies have identified adverse childhood experiences including sexual, physical, and emotional abuse as risk factors for non-fatal and fatal overdose (Cutajar et al., 2010; Lake et al., 2015). Our findings provide evidence for the ability of less severe adverse childhood exposures, including parental heavy drinking, to negatively impact subsequent adult health outcomes. Given the increasing evidence of the negative impact of adverse childhood experiences, ensuring all parents have access to programs and services focusing on improving parenting skills and providing social and/or emotional support to reduce child maltreatment is essential (Van der Put, Assink, Gubbels, & Boekhout van Solinge, 2017). As parental heavy drinking may also be an indication of alcohol use disorders, improving access to appropriate treatment programs is necessary. Further, within adult drug using populations expanding counseling services addressing childhood vulnerabilities and building positive coping skills may aid in reducing overdose risks.

As our study population is comprised of adults, parental heavy drinking was often experienced decades before reported non-fatal overdoses and as such there are many potential pathways involved. Pathways previously identified linking exposure to parents with alcohol use disorder and negative health outcomes involve social and biological factors, which research indicates may be similar pathways for less severe parental alcohol misuse, including heavy drinking (Mares, van der Vorst, Engels, & Lichtwarck-Aschoff, 2011). For parents, heavy drinking may be a coping mechanism for depressive symptoms and low social support resulting in supervisory neglect towards children (Lloyd & Kepple, 2017). In turn, supervisory neglect may lead to not only juvenile delinquency but also decreased educational attainment and consequently reduced employment opportunities resulting in psychological distress (Bijttebier & Goethals, 2006; Snyder & Merritt, 2015). Previous studies also identified an association between parental drinking and dysfunctional family environments, including low family cohesion, negatively influencing adolescent adjustment and increased psychological distress (Bijttebier & Goethals, 2006; Finan et al., 2015). In order to cope with the psychological distress, directly and indirectly resulting from parental heavy drinking, adolescents and adults may adapt harmful health behaviours, including risky drug use known to increase overdose risk. Additionally, psychological distress may increase severe depressive symptoms leading to an increased overdose risk through a decreased ability to engage in emotional-regulation strategies (Pabayo et al., 2013). Finally, parental heavy drinking may also indicate mothers who drank during pregnancy resulting in fetal alcohol syndrome with long-term impacts including compulsive behaviours and substance use disorders increasing overdose risk (Behnke & Smith, 2013).

Currently, illicit drug overdose programs overwhelmingly focus on distribution and education of naloxone use, awareness campaigns for signs of overdose among users, and the use of supervised consumption sites (Clark, Wilder, & Winstanley, 2014; Kennedy, Karamouzian, & Kerr, 2017; Winstanley, Clark, Feinberg, & Wilder, 2016). While essential to reduce overdose mortality, these programs do not address life course vulnerabilities

influencing drug use and may be missing opportunities for earlier interventions. Our research points to the need for a scale-up of early intervention programs targeting children at high risk of maltreatment prior to problematic drug or alcohol use. Future research should also investigate the cost-effectiveness of programs for at-risk children. This could provide the needed evidence for policy makers to make informed decisions regarding public health spending.

This study has several limitations. First, the VIDUS and ACCESS cohorts are not random samples and therefore generalizability of the findings may be limited. As the study setting of Vancouver is currently facing an unprecedented overdose crisis, generalizability may be further limited when considering communities not facing a similar crisis, as the low rates of overdose in those communities may potentially lead to non-significant associations. Second, data used in the study, including those for the primary explanatory and outcome variables, were solely based on self-report and thus could be subject to reporting bias, including socially desirable responses. However, self-reported behavioural data has been shown to be largely accurate among adult drug-using populations (Darke, 1998). Further, as the primary explanatory variable is a historical variable, concerns with recall bias and socially desirable responding are possible. Based on the limitation of our dataset we were unable to quantify the frequency or extent of parental alcohol use and resulting impacts on family functioning; we were also unable to determine if the person they lived with most was considered a parental figure. Incorporating additional variables to capture parental problem heavy drinking is an area for future research. These could include additional questions regarding the extent to which the participant knew about their parent's drinking when they were children, whether they viewed their parent as a parental figure, and the extent to which the heavy drinking impacted the family. Further, a future study could involve parent-child dyads beginning in adolescence and followed until the child reaches adulthood. At baseline the child could be questioned regarding their knowledge of parental heavy drinking, with a parental interview separately conducted to corroborate drinking information, similar to previous studies investigating the impact of parental behaviours on children (Lund et al., 2015; Vermeulen-Smit et al., 2012). Lastly, as with any observational research, unmeasured confounders may exist although we sought to reduce this bias through adjustment of statistical models using key predictors of non-fatal overdose. As this was an observational study we cannot infer causation between parental heavy drinking and non-fatal overdose.

## 5. CONCLUSION

In summary, our findings demonstrated high rates of exposure to parental heavy drinking among our sample of people who inject drugs. We also found that parental heavy drinking remained independently associated with recent non-fatal overdose after adjusting for relevant socio-demographic and drug using confounders. These findings demonstrate the need to expand on parenting interventions to decrease child maltreatment to prevent future health impacts. In light of the ongoing overdose crisis future research aimed at identifying effective interventions addressing vulnerabilities introduced during childhood is imperative to prevent the devastating impacts of overdose.

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## ABBREVIATIONS

<b>DTES</b>	Downtown Eastside
<b>HIV</b>	Human immunodeficiency virus

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### HIGHLIGHTS

- We investigated the impact of parental heavy drinking on non-fatal overdose.
- The prevalence of parental heavy drinking among people who inject drugs is high.
- Parental heavy drinking was associated with an increased risk of non-fatal overdose.

**Table 1:**

Baseline sample characteristics, stratified by non-fatal overdose in the past six months among people who inject drugs in Vancouver, Canada (n = 327).

Characteristic	Non-fatal overdose *		<i>p</i> - value
	Yes n (%) 47 (14.4)	No n (%) 280 (85.6)	
Parental heavy drinking	26 (55.3)	85 (30.4)	0.001
Age (median, IQR)	34 (31–37)	37 (31–46)	0.046
Female sex	21 (44.7)	126 (45.0)	0.968
White	28 (59.6)	135 (48.2)	0.149
Homeless *	33 (70.2)	109 (38.9)	<0.001
DTES residency *	44 (93.6)	203 (72.5)	0.001
Daily injection heroin use *	23 (48.9)	79 (28.2)	0.005
Daily injection stimulant use *	18 (38.3)	54 (19.3)	0.004
Incarceration *	12 (25.5)	31 (11.1)	0.007
Engaged in OAT *	23 (48.9)	134 (47.9)	0.908
HIV positive	9 (19.1)	137 (48.9)	<0.001

CI: confidence interval; IQR: interquartile range; DTES: Downtown Eastside; OAT: opioid agonist therapy

\* Denotes activities in the previous six months.

**Table 2.**

Bivariable and multivariable GEE analysis of non-fatal overdose among people who inject drugs in Vancouver, Canada (n = 327).

Characteristic	Unadjusted non-fatal overdose		Adjusted non-fatal overdose <sup>†</sup>	
	Odds Ratio (95% CI)	p - value	Odds Ratio (95% CI)	p - value
<b>Parental heavy drinking</b>				
(yes vs. no)	1.66 (1.05–2.62)	0.028	1.69 (1.07–2.66)	0.023
<b>Age</b>				
(per year older)	0.96 (0.94–0.99)	0.003		
<b>Sex</b>				
(Female vs. male)	0.85 (0.54–1.33)	0.477		
<b>Ethnicity</b>				
(White vs. other)	1.13 (0.72–1.76)	0.600		
<b>Homelessness *</b>				
(yes vs. no)	2.38 (1.56–3.64)	<0.001	2.20 (1.41–3.44)	0.001
<b>DTES residency *</b>				
(yes vs. no)	1.13 (0.72–1.78)	0.597		
<b>Daily injection heroin use *</b>				
(yes vs. no)	2.21 (1.52–3.20)	<0.001		
<b>Daily injection stimulant use *</b>				
(yes vs. no)	2.00 (1.36–2.93)	<0.001		
<b>Incarceration *</b>				
(yes vs. no)	2.10 (1.17–3.79)	0.013		
<b>Engaged in OAT *</b>				
(yes vs. no)	0.81 (0.54–1.21)	0.302		
<b>HIV Serostatus</b>				
(positive vs. negative)	0.33 (0.21–0.53)	<0.001	0.40 (0.25–0.63)	<0.001

GEE: generalized estimating equations; CI: confidence interval; DTES: Downtown Eastside; OAT: opioid agonist therapy

\* Denotes activities in the previous six months.

<sup>†</sup> Although all secondary explanatory variables from the bivariable analysis were eligible for inclusion in the final model, only those that affected the estimate of the main exposure variable—childhood emotional abuse—by 5% were included in the final adjusted model.