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Association between posttraumatic stress disorder and non-fatal drug overdose

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Abstract

Objective: North America is in the midst of a growing drug overdose crisis. While prescription opioid misuse and synthetic opioids such as fentanyl have been implicated in the overdose crisis, less attention has been given to the role that post-traumatic stress disorder (PTSD) may play in this crisis. As such, this study sought to examine the relationship between PTSD and risk of non-fatal overdose among people who use drugs (PWUD).

Methods: Data were derived from three prospective cohorts of PWUD in Vancouver, Canada. For each participant, PTSD was assessed using the PTSD Checklist for the DSM-V. Multivariate logistic regression analyses was used to estimate the relationship between PTSD and non-fatal overdose, adjusting for potential confounders.

Results: Between 2016 and 2018 among 1059 PWUD, including 363 (34%) non-male participants, 171 (16%) experienced a non-fatal drug overdose in the past six months, and 414 (39%) met criteria for a provisional PTSD diagnosis. In multivariate analysis, PTSD (Adjusted Odds Ratio [AOR] = 1.98, 95% confidence interval [CI]: 1.41 – 2.79) remained independently associated with non-fatal overdose after adjustment for a range of confounders.

Conclusions: Among participants in these community-recruited cohorts of PWUD, having a provisional PTSD diagnosis nearly doubled the risk of non-fatal overdose. The findings from this study support the need to incorporate a trauma-informed approach within the current overdose prevention framework. Education and training relating to trauma and PTSD should be prioritized for healthcare professionals who work with and treat PWUD.

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Keywords

Posttraumatic stress disorder; illicit drug use; drug overdose; mental health

The United States and Canada is currently facing crises of opioid use and overdose, with mortality rates in the United States reaching 19.8 deaths per 100,000 individuals, marking a 21% increase from 2015 to 2016 (Hedegaard, Warner, & Minino, 2017). The Canadian province of British Columbia (BC) declared a public health emergency in 2016, where illicit drug overdose rates have reached 31deaths per 100,000 in 2018 (Government of British Columbia, 2018). With 1,458 recorded deaths in BC alone in 2017, the overdose crisis has quickly become one of the most pressing public health challenges. **Illicitly-manufactured synthetic opioids, such as fentanyl, account for a substantial number of these overdose deaths (British Columbia Coroners Service, 2017a), and these fatalities can be attributed to the fact that fentanyl has been found in supplies of both opioid and non-opioid street drugs, such as cocaine and methamphetamines (Miller and Russell, 2016). Furthermore, a recent study showed that methamphetamine and cocaine use – in addition to morphine and heroin – were positively associated with fentanyl exposure (Hayashi et al., 2018). Given the known presence of fentanyl in the illicit drug supply, and the fact that the risk of overdose is not exclusive to opioid use, it is incumbent on researchers and clinicians to consider prevention initiatives that help people who use illicit drugs (PWUD) of any kind, in an effort to curtail the progression of this health crisis.**

The ensuing response has been centered around harm-reduction strategies, including expansion of supervised consumption sites, take-home naloxone kits, and opioid agonist treatment, given past evidence supporting the effectiveness of such interventions in mitigating overdose fatalities (Fairgrieve, Fairbairn, Samet, & Nolan, 2018; Lake, & Milloy, 2018; Morgan, & Jones, 2018; Young, & Fairbairn, 2018). Despite these efforts, the number of overdose deaths in the province continue to rise, marked by a 4.5% increase in average monthly overdose fatalities from 2017 (122 deaths) to 2018 (127 deaths) (Government of British Columbia, 2018). **It is of commensurate importance to acknowledge cases involving non-fatal drug overdose, as it is several times more common than overdose resulting in death (CDC's Enhanced State Opioid Overdose Surveillance Program, 2018), and is a strong risk factor for early mortality among PWUD** (Caudarella, et al., 2016). **Not only does non-fatal overdose lend itself to a plethora of health issues, including acquired brain injuries, muscular dysfunction, and renal failure** (Darke, & Hall, 2003; Britton, Wines, & Conner, 2010), **but it also presents a significant social and economic burden on communities and the healthcare system (Hagemeier, 2018).**

In light of this growing public health challenge, additional efforts should be made to identify other factors with potential to exacerbate this health crisis. One possible factor that warrants consideration is posttraumatic stress disorder (PTSD), given the well-known association between PTSD and substance use (Elwyn, & Smith, 2013; Driessen et al., 2008; Levenson, Willis, & Prescott, 2016). For example, those diagnosed with PTSD exhibit significantly higher rates of substance use than those without PTSD (Klimkiewicz, Klimkiewicz,

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Jakubczyk, Kieres-Salomonksi, & Wojnar, 2015; Goldstein et al., 2016) and the prevalence of PTSD among people with substance use disorder ranges from 30 – 60%, **compared to a prevalence of 5 – 9% in the general North American population** (Goldstein et al., 2016; **McCauley et al., 2017;** Roberts, Roberts, Jones, & Bisson, 2015; Van Ameringen, Mancini, Patteron, & Boyl, 2008). These findings are not surprising given that PTSD symptomology, which includes intrusive cognitions and impulsivity associated with trauma, may promote maladaptive coping behaviors **that lead to worse health outcomes**, including substance use (Weiss, Tull, Viana, Anestis, & Gratz, 2012). The consequences of such comorbidity have been historically documented, with individuals with two or more concurrent conditions often exhibiting more severe and prolonged symptomatology, higher reports of disability, and frequent interactions with the judicial system (Kessler et al., 1994; Leveson, & Socia, 2016; Merikangas et al., 2003; Roy-Byrne et al., 2000), relative to non-comorbid samples. **Furthermore, another study showed that this concurrency can have direct life-threatening outcomes, in that PTSD diagnosis was associated with non-fatal drug overdose among a rural sample of PWUD** (Havens, et al., 2011).

A prominent theory that elucidates the relationship between psychiatric disorder and drug use is the self-medication hypothesis (Khantzian, 1997): a psychodynamic model for addiction that highlights the role of substances as agents of relief from psychological distress associated with, for example, PTSD. Evidence supporting this theory is substantial, where studies have demonstrated that PTSD symptom severity predicted increased drug cravings (Coffey et al., 2002), and more specifically, that an individual's drug of choice is reflected in their PTSD symptom cluster severity (Lazareck et al., 2012). Accordingly, drug cravings and drug use were shown to decrease following trauma-focused therapy (Saladin et al., 2003). Further, there is research that corroborates a neurobiological basis for the self-medication hypothesis (Awad, & Voruganti, 2015), Further, there is research that corroborates a neurobiological basis for the self-medication hypothesis, **where present neuroimaging technology has demonstrated that the neurotransmitter effects resulting from, for example, PTSD, can affect someone's drug use** (Awad, & Voruganti, 2015).

Although the increased risk for comorbid substance use and PTSD has been documented, little is known about the impact of PTSD in the context of the current opioid overdose crisis, especially in non-clinical urban settings and among non-veteran populations. Given the potential influence of psychological mechanisms on substance use, there is a need for research to clarify the relationship between mental health and drug overdose amidst a plethora of other social-structural drivers of this crisis, including homelessness and incarceration. Specifically, the primary aim of the study was to investigate whether PTSD was independently associated with non-fatal overdose, among people who use drugs (PWUD) in Vancouver, Canada. This study hypothesized that there would be an independent relationship between **provisional** PTSD **diagnosis** and non-fatal drug overdose, controlling for relevant confounders.

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Methods

Participants and procedures

From December 2016 to November 2018, cross-sectional data were collected from the Vancouver Injection Drug User Study (VIDUS), the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS) and the At-Risk Youth Study (ARYS); three open ongoing prospective cohort studies of PWUD in Vancouver, Canada. These cohorts have been described in detail previously (Urban Health Research Institute, 2013; Wood, Stoltz, Montaner, & Kerr, 2006). In brief, study participants were recruited through community outreach since May 1996. VIDUS is a cohort study of HIV-negative adult PWUD who have reported any injection drug use in the previous month before baseline. ACCESS is a cohort of HIV-positive adult PWUD who report any illicit drug use (not including cannabis, which was legalized in October, 2018) in the month before baseline. Finally, ARYS is a cohort study of street-involved youth aged 14–26 years at time of recruitment, and had reported any illicit drug use, except for cannabis, in the month before baseline. All eligible participants provide written and informed consent. The three studies employ harmonized data collection and follow-up processes to allow for combined analyses. Specifically, at baseline and semi-annually thereafter, study participants answer an interviewer-administered questionnaire that elicits information about socio-demographic characteristics, drug-use patterns, engagement with health-care services and law enforcement, and other behavioral and contextual factors. They were also asked to provide biological samples, including blood samples for serological testing or HIV clinical monitoring (where applicable) and urine testing for initial drug screens. Participants received $40 CAD for each study visit. Additionally, all participants for the present study were asked to answer a supplemental questionnaire that assesses for *DSM*-V PTSD symptomology, and lifetime traumatic exposure. Participants provided informed consent, and were compensated an additional $15 CAD.

Measures

The primary outcome of this study was having experienced at least one non-fatal drug overdose in the previous six months. Since polysubstance drug use is the norm across our cohorts, and because we were interested in overdoses involving any substance, we used a broad definition of non-fatal drug overdose by asking participants: “In the last 6 months, have you overdosed by accident (i.e., where you had a negative reaction from using too much drugs or had a bad trip)?”. Participants who responded “yes” were defined as experiencing a non-fatal overdose in all subsequent analyses. This definition was pilot tested during questionnaire development, and has been used in previous studies involving PWUD (Kerr et al., 2007; Pabayo, Alcantara, Kawachi, Wood, & Kerr, 2013).

The primary explanatory variable of interest was having a provisional PTSD diagnosis. This information was ascertained by using the PTSD Checklist for *DSM*-V (PCL-5), a 20-item self-report measure that assesses the 20 *DSM*-V symptoms of PTSD **in the previous month** (Blevins, Weathers, Davis, Witte, & Domino, 2015). **This version of the PCL-5 included the revised Life Events Checklist for DSM-V, and an extended Criterion A assessment. To ensure data accuracy and study participants’ emotional well-being, specially-trained research interviewers with backgrounds in counselling psychology**

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administered this format of the PCL-5 assessment. Each of the 20 items (e.g., "In the past month, how much were you bothered by repeated, disturbing, and unwanted memories of the stressful experience?") consist of a five-point Likert response (0 = "not at all" to 4 = "extremely") measuring severity of the specific PTSD symptom. The total score ranges from 0–80, with signal detection analyses using the Clinician-Administered PTSD Scale for *DSM*-V – the gold standard for PTSD diagnosis – indicating a cut-point score of ≥31 (k[0.5]=0.58) as an accurate predictor for probable PTSD diagnosis (Bovin et al., 2015). **Among our current sample of PWUD, the Cronbach's alpha for the 20 PTSD symptom items was 0.96.** The PCL-5 **also** yielded good test-retest reliability (r=0.84) (Blevins, Weathers, Davis, Witte, & Domino, 2015).

Secondary variables hypothesized to be potential confounders included: age (median split); gender (male vs. non-male); ethnicity (white vs. non-white); homelessness (yes vs. no); needed help injecting (yes vs. no); injected in public (yes vs. no); daily heroin injection (yes vs. no); daily stimulant injection (yes vs. no); daily illicit prescription opioid use (yes vs. no); daily alcohol use (yes vs. no); incarceration (yes vs. no), and accessed opioid agonist treatment (yes vs. no). All time-varying variables are time-updated and refer to the six-month period prior to follow-up interview, unless otherwise stated.

Statistical Analyses

As a first step, the characteristics of the explanatory variables were examined, stratified by non-fatal overdose. Specifically, Pearson's chi-square test for dichotomous variables were used to assess the relations among the characteristics and non-fatal overdose. Bivariate logistic regression analyses were then used to assess the association between each explanatory variable and non-fatal overdose. Next, to fit the multivariate model to estimate the effect of PTSD on the risk of non-fatal overdose, model selection approach (Maldonado, 1993) was employed where we included all potential confounders (where $p<0.10$ in the bivariate analysis) in the full multivariate model and used a stepwise approach to fit a series of reduced models. After comparing the value of the coefficient associated with PTSD in the full model to the value of the coefficient in each of the reduced models, the secondary variables associated with the smallest relative change were dropped. This iterative process was continued until the minimum change exceeded 5%. Remaining variables were considered confounders in the multivariate analysis. All statistical analyses were performed using SAS 9.4 (SAS, Cary, North Carolina, United States). All p-values are two sided.

Results

Of the 1059 PWUD included in the present study, 363 (34%) were non-male, and the median age at the time of interview was 45 years (Interquartile Ratio [IQR]: 31.10 – 54.30). In total, 414 (39%) met the provisional diagnostic criteria for PTSD, and 171 (16%) had experienced a non-fatal overdose. Among those who had PTSD, 94 (23%) experienced a non-fatal overdose. The characteristics of the study sample stratified by non-fatal drug overdose are presented in Table 1. In bivariate analysis, PTSD was associated with higher odds of non-fatal overdose (Odds Ratio = 2.17, 95% confidence interval [CI]: 1.56 – 3.02). Additionally, bivariate analyses showed that younger age, homelessness, needing help

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injecting drugs, public injection drug use, daily injection heroin use, daily injection stimulant use, daily prescription opioid use, and incarceration were positively associated with non-fatal drug overdose (all $p < 0.05$). In a multivariate logistic regression analysis, PTSD (Adjusted Odds Ratio [AOR] = 1.98, 95% CI: 1.41 – 2.79) remained independently associated with higher odds of non-fatal drug overdose, in the presence of other variables. Results from the bivariate and multivariate analyses examining the factors associated with non-fatal drug overdose are presented in Table 2.

Discussion

The current study found that PTSD was common among our community-based sample of PWUD, with approximately 40% of participants having met provisional diagnostic criteria for PTSD, and about 16% had experienced a non-fatal drug overdose in the past six months. After adjusting for a range of relevant confounders, PTSD diagnosis was associated with significantly higher odds of experiencing a non-fatal overdose, compared with those who did not have PTSD. This study is among the first to demonstrate that PTSD is linked to a greater risk of drug overdose.

These findings mirror the growing body of literature that demonstrates an elevated prevalence of PTSD among PWUD compared to non-PWUD populations. The link between PTSD and substance use has been well-established (Breslau, Davis, & Peterson, 1991; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; McCauley et al., 2012; Persson et al., 2017) and has been widely considered as a reflection of the self-medication theory (Awad & Vorunganti, 2015; Coffey et al., 2002; Khantzian, 1997; Lazareck et al., 2012; Saladin et al., 2003;), whereby substance use alleviates or suppresses symptoms of PTSD. Accordingly, this study suggests that non-fatal overdose is not simply an adverse outcome of substance use, but may in fact be attributable to psychopathology associated with PTSD. This claim is supported by previous studies which found that childhood traumatic experiences were associated with non-fatal overdose among PWUD (Lake et al., 2015; Braitstein et al., 2003), which could partially reflect attempts at self-medication as a means of coping with PTSD symptoms that subsequently lead to overdose. For example, the avoidance of trauma-related cues could elicit an urgency to seek and use substances for its acute psychoactive effects, such as anti-panic and anti-anxiety, to alleviate the emotional pain associated with the trauma (Dworkin, Wanklyn, Stasiewicz, & Coffey, 2018; Pizzimenti, Navis, & Lattal, 2017). However, as a result, a harmful feedback loop can occur such that increased drug use itself can exacerbate psychiatric symptomology (Garland, Pettus-Davis, & Howard, 2013), which ultimately renders the traumatized PWUD at higher risk for overdose, especially when the substance of choice is a central nervous system depressant such as heroin or another opioid. An important consideration to note is the recently renewed scientific interest in psychedelic medicine (e.g., methylenedioxymethamphetamine) for treating PTSD (Tupper, Wood, Yensen, & Johnson, 2015), which has shown successful preliminary clinical outcomes and therapeutic efficacy with few adverse side effects (Ot'alora et al., 2018; Mithoefer, et al., 2011; Mithoefer et al., 2013). Other forms of substances, such as cannabinoids, have also been investigated for its therapeutic utility and yielded similar results (Loflin, Babson, & Bonn-Miller, 2017; Passie, Emrich, Karst, Brandt, & Halpern, 2012). These studies abate the notion that all drugs engender increased risk of worsening psychological symptoms and

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subsequent overdose among those who have PTSD, and instead suggests that there may be certain psychoactive substances that can serve as a potential adjunct to the current conventional models of PTSD treatment, and not pose as a hindrance for recovery. Given that this research is still in its infancy, further studies are required to better understand the potential impact of psychedelics and cannabis in the addiction treatment and overdose prevention context for those with PTSD.

Despite the dissemination of public health campaigns promoting safer drug-use practices and overdose prevention strategies in our setting and some others (Government of British Columbia, 2018), the effectiveness of such strategies rely largely on the ability and willingness of PWUD to engage in those prevention behaviors. However, the symptoms of PTSD, characterized by intrusions, avoidance, mood alterations and hyperarousal (American Psychiatric Association, 2013), can affect the ability to cognitively and emotionally self-regulate, and thereby compromise the desire or capacity to engage in those harm-reduction efforts. Previous studies have illustrated this phenomenon (Ehring, & Quack, 2010; Tull et al., 2016), where PTSD symptom strength was shown to predict the inability to control impulsive behaviors when distressed, as well as constrain goal-directed behaviors. Also of concern is research implicating emotional suffering as a factor that directly undermines the intentions of PWUD to engage in safer behaviors (Kerr, Small, Hyshka, Maher, & Shannon, 2013). In other words, although PWUD were aware of the available services and strategies for safer drug use practices, priority may have been given to, for instance, relieving emotional pain, despite the consequentially increased risk of overdose. Indeed, past work has highlighted the issue of ambivalence towards death among PWUD, and the link between trauma and suicidal behaviors has been well-described (Gradus et al., 2010; LeBouthillier, McMillan, Thibodeau, & Asmundson, 2015). In light of the various potential explanatory pathways, it is clear that the relationship between PTSD and drug overdose highlights the need to prioritize the availability and accessibility of mental health services, including counselling and trauma-focused support groups, for PWUD in order to mitigate overdose risk.

This study has several noteworthy strengths. First, it used a large sample of community-based PWUD, which differs from veteran and clinically-based populations that were more commonly observed in PTSD research. Next, this study was among the first of its kind to investigate the potential psychopathological drivers of the current overdose crisis in the United States and Canada. Finally, the primary explanatory variable was ascertained by clinically-trained research interviewers administering a validated measure for PTSD, which strengthens the accuracy of the study's findings. This differs from many studies examining traumatic stress in relation to substance use, in that assumptions about manifested psychological symptoms were made, rather than objectively verified (e.g., use of instrument assessing childhood traumatic experiences as a means of ascertaining PTSD severity). Still, this study also has limitations. First, the study cohorts are not random samples, and thus findings may not be fully generalizable to other drug-using populations. Second, participant data was ascertained by self-report, and was therefore subject to response biases, including social desirability. Lastly, this study was cross-sectional in nature, which prevents any conclusions drawn about cause and effect.

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In sum, this study found that more than a third of PWUD met provisional diagnosis for PTSD, and that PTSD was independently and significantly associated with non-fatal drug overdose. These findings highlight the need for clinical settings to bolster availability and access to mental health services to reduce adverse psychological outcomes associated with overdose. **For example, low-barrier psychological treatments that include free therapy sessions and education, and access to trauma-centered therapy, should be made readily available at services frequented by PWUD, including supervised injection facilities and health clinics.** Additionally, engaging in educational training around the use of brief screening measures that assess for PTSD is highly recommended for healthcare professionals working with and treating PWUD. Future research should examine longitudinal associations between PTSD and drug overdose, and should also examine the associations between PTSD symptom cluster severity and preferred substance use, with the aim of tailoring treatment that is specific to the needs of community-based PWUD, while also shedding light on the etiological basis of drug use and mental health.

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References

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed). Arlington, VA: Author

Awad AG, & Voruganti LL (2015). Revisiting the 'self-medication' hypothesis in light of the new data linking low striatal dopamine to comorbid addictive behavior. Therapeutic Advances in Psychopharmacology, 5, 172–178. 10.1177/2045125315583820 [PubMed: 26199720]

Blevins CA, Weathers FW, Davis MT, Witte TK, & Domino JL (2015). The posttraumatic stress disorder checklist for DSM-5 (PCL-5): Development and initial psychometric evaluation. Journal of Traumatic Stress, 28, 489–498. 10.1002/jts.22059 [PubMed: 26606250]

Bovin MJ, Marx BP, Weathers FW, Gallagher MW, Rodriguez P, Schnurr PP, & Keane TM (2015). Psychometric properties of the PTSD Checklist for diagnostic and statistical manual of mental disorders-fifth edition (PCL-5) in veterans. Psychological Assessment, 28, 1379–1391. 10.1037/pas0000254 [PubMed: 26653052]

Braitstein P, Li K, Tyndall M, Spittal P, O'Shaughnessy MV, Schilder A, & Schechter MT (2003). Sexual violence among a cohort of injection drug users. Social Science and Medicine, 57, 561–569. 10.1016/s0277-9536(02)00403-3. [PubMed: 12791497]

Breslau N, Davis GC, Andreski P, & Peterson E (1991). Traumatic events and posttraumatic stress disorder in an urban population of young adults. Archives of General Psychiatry, 48, 216–222. doi:10.1001/archpsyc.1991.01810270028003 [PubMed: 1996917]

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Britton PC, Wines JD Jr, & Conner KR (2010). Non-fatal overdose in the 12 months following treatment for substance use disorders. Drug and Alcohol Dependence, 107, 51–55. https://doi.org/10.1016Zj.drugalcdep.2009.09.005 [PubMed: 19828263]

Caudarella A, Dong H, Milloy MJ, Kerr T, Wood E, & Hayashi K (2016). Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. Drug and Alcohol Dependence, 162, 51–55. https://doi.org/10.10167j.drugalcdep.2016.02.024 [PubMed: 26993373]

Coffey SF, Saladin ME, Drobes DJ, Brady KT, Dansky BS, & Kilpatrick DG (2002). Trauma and substance cue reactivity in individuals with comorbid posttraumatic stress disorder and cocaine or alcohol dependence. Drug and Alcohol Dependence, 65, 115–127. 10.1016/S0376-8716(01)00157-0 [PubMed: 11772473]

Driessen M, Schulte S, Luedecke C, Schaefer I, Sutmann F, Ohlmeier M, Kemper U, Koesters G, Chodzinski C, Schneider U, & Broese T (2008). Trauma and PTSD in patients with alcohol, drug, or dual dependence: a multi-center study. Alcoholism: Clinical and Experimental Research, 32, 481–488. 10.1111/j.15300277.2007.00591.x

Darke S, & Hall W (2003). Heroin overdose: Research and evidence-based intervention. Journal of Urban Health, 80, 189–200. [PubMed: 12791795]

Dworkin ER, Wanklyn S, Stasiewicz PR, & Coffey SF (2018). PTSD symptom presentation among people with alcohol and drug use disorders: Comparisons by substance of abuse. Addictive Behaviors, 76, 188–194. https://doi.org/10.1016Zj.addbeh.2017.08.019 [PubMed: 28846939]

Ehring T, & Quack D (2010). Emotion regulation difficulties in trauma survivors: The role of trauma type and PTSD symptom severity. Behavior Therapy, 41, 587–598. 10.1016/j.beth.2010.04.004 [PubMed: 21035621]

Elwyn L, & Smith C (2013). Child maltreatment and adult substance abuse: The role of memory. Journal of Social Work Practice in the Addictions, 13, 269–294. 10.1080/1533256X.2013.814483

Fairgrieve C, Fairbairn N, Samet JH, & Nolan S (2018). Nontraditional alcohol and opioid agonist treatment interventions. Medical Clinics of North America, 102, 683–96. https://doi.org/10.1016Zj.mcna.2018.02.006 [PubMed: 29933823]

Garland EL, Pettus-Davis C, & Howard MO (2013). Self-medication among traumatized youth: Structural equation modeling of pathways between trauma history, substance misuse, and psychological distress. Journal of Behavioral Medicine, 36, 175–185. 10.1007/s10865-012-9413-5 [PubMed: 22454227]

Goldstein RB, et al. (2016). The epidemiology of DSM-5 posttraumatic stress disorder in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Social Psychiatry and Psychiatric Epidemiology, 51, 1137–1148. doi: 10.1007/s00127-016-1208-5 [PubMed: 27106853]

Government of British Columbia. (2018). Illicit drug overdose deaths in BC, January 1, 2008 – September 30, 2018. BC Coroners Service Report. Accessed on December 3rd, 2018 Available at: https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf

Government of British Columbia. (2018). Responding to British Columbia's illegal drug overdose epidemic. British Columbia Ministry of Mental Health and Addictions. Accessed on December 20th, 2018 Available at: https://www2.gov.bc.ca/assets/gov/overdose-awareness/final_responding_to_bcs_opioid_overdose_epidemic_-_progress_updatejan_2018.pdf

Gradus JL, Qin P, Lincoln AK, Miller M, Lawler E, Sørensen HT, & Lash TL (2010). Posttraumatic stress disorder and completed suicide. American Journal of Epidemiology, 171, 721–727. 10.1093/aje/kwp456 [PubMed: 20160171]

Havens JR, Oser CB, Knudsen HK, Lofwall M, Stoops WW, Walsh SL, Leukefeld CG, & Kral AH (2011). Individual and network factors associated with non-fatal overdose among rural Appalachian drug users. Drug and Alcohol Dependence, 115, 107–112. https://doi.org/10.1016Zj.drugalcdep.2010.11.003 [PubMed: 21126831]

Hedegaard H, Warner M, & Minino AM (2017) Drug overdose deaths in the United States, 1999–2016. NCHS Data Brief 294, 1–8.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Kerr T, Fairbairn N, Tyndall M, Marsh D, Li K, Montaner J, & Wood E (2007). Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. Drug and Alcohol Dependence, 87, 39–45. 10.1016/j.drugalcdep.2006.07.009 [PubMed: 16959438]

Kerr T, Small W, Hyshka E, Maher L, & Shannon K (2013). It's more about the heroin: Injection drug users' response to an overdose warning campaign in a Canadian setting. Addiction, 108, 1270–1276. 10.1111/add.12151 [PubMed: 23551565]

Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, & Kendler KS (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Survey. Archives of General Psychiatry, 51, 8–19. 10.1001/archpsyc.1994.03950010008002 [PubMed: 8279933]

Kessler RC, Sonnega A, Bromet E, Hughes M, & Nelson CB (1995). Posttraumatic stress disorder in the National Comorbidity Survey. Archives of General Psychiatry, 52, 1048–1060. doi:10.1001/archpsyc.1995.03950240066012 [PubMed: 7492257]

Klimkiewicz A, Klimkiewicz J, Jakubczyk A, Kieres-Salomonski I, & Wojnar M (2015). Comorbidity of alcohol dependence with other psychiatric disorders. Part I. Epidemiology of dual diagnosis. PsychiatriaPolska, 49, 265–275. 10.12740/PP/25704

Khantzian EJ (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. Harvard Review Psychiatry, 4, 231–244.

Lake S, Hayashi K, Milloy MJ, Wood E, Dong H, Montaner J, & Kerr T (2015). Associations between childhood trauma and non-fatal overdose among people who inject drugs. Addictive Behaviors, 43, 83–88. https://doi.org/10.10167j.addbeh.2014.12.014 [PubMed: 25588793]

Lake S, & Milloy MJ (2018). Access to medical cannabis is expanding across North America regardless of the opioid crisis—why not study if it could help?. Addiction, 113, 1550–1551. 10.1111/add.14236 [PubMed: 29882263]

Lazareck S, Robinson J, Crum RM, Mojtabai R, Sareen J, & Bolton JM (2012). A longitudinal investigation of the role of self-medication in the development of comorbid mood and drug use disorders. The Journal of Clinical Psychiatry, 73, e588–e593. 10.4088/JCP.11m07345 [PubMed: 22697205]

LeBouthillier DM, McMillan KA, Thibodeau MA, & Asmundson GJ (2015). Types and number of traumas associated with suicidal ideation and suicide attempts in PTSD: Findings from a US nationally representative sample. Journal of Traumatic Stress, 28, 183–190. 10.1002/jts.22010 [PubMed: 25990916]

Levenson JS, & Socia KM (2016). Adverse childhood experiences and arrest patterns in a sample of sexual offenders. Journal of Interpersonal Violence, 31, 1883–1911. 10.1177/0886260515570751 [PubMed: 25711615]

Levenson JS, Willis GM, & Prescott DS (2016). Adverse childhood experiences in the lives of male sex offenders: Implications for trauma-informed care. Sexual Abuse, 28, 340–359. 10.1177/1079063214535819 [PubMed: 24872347]

Loflin MJ, Babson KA, & Bonn-Miller MO (2017). Cannabinoids as therapeutic for PTSD. Current Opinion in Psychology, 14, 78–83. https://doi.org/10.1016Zj.copsyc.2016.12.001 [PubMed: 28813324]

Maldonado G, & Greenland S (1993). Simulation study of confounder-selection strategies. American Journal of Epidemiology, 138, 923–936. 10.1093/oxfordjournals.aje.a116813 [PubMed: 8256780]

McCauley JL, Killeen T, Gros DF, Brady KT, & Back SE (2012). Posttraumatic stress disorder and cooccurring substance use disorders: Advances in assessment and treatment. Clinical Psychology: Science and Practice, 19, 283–304. 10.1111/cpsp.12006

Merikangas KR, Zhang H, Avenevoli S, Acharyya S, Neuenschwander M, Angst J (2003). Longitudinal trajectories of depression and anxiety in a prospective community study: The Zurich Cohort Study. Archives of General Psychiatry, 60, 993–1000. doi:10.1001/archpsyc.60.9.993 [PubMed: 14557144]

Mithoefer MC, Wagner MT, Mithoefer AT, Jerome L, & Doblin R (2011). The safety and efficacy of 3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: The first randomized controlled pilot study. Journal of Psychopharmacology, 25, 439–452. 10.1177/0269881110378371 [PubMed: 20643699]

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Mithoefer MC, Wagner MT, Mithoefer AT, et al. (2013). Durability of improvement in posttraumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: A prospective long-term follow-up study. Journal of Psychopharmacology, 27, 28–39. 10.1177/0269881112456611 [PubMed: 23172889]

Morgan J, & Jones AL (2018). The role of naloxone in the opioid crisis. Toxicology Communications, 2, 15–18. 10.1080/24734306.2018.1458464

Ot'alora GM, Grigsby J, Poulter B, et al. (2018). 3, 4-Methylenedioxymethamphetamine- assisted psychotherapy for treatment of chronic posttraumatic stress disorder: A randomized phase 2 controlled trial. Journal of Psychopharmacology, 32, 1295–1307. 10.1177/0269881118806297 [PubMed: 30371148]

Pabayo R, Alcantara C, Kawachi I, Wood E, & Kerr T (2013). The role of depression and social support in non-fatal drug overdose among a cohort of injection drug users in a Canadian setting. Drug and Alcohol Dependence, 132, 603–609. https://doi.org/10.1016Zj.drugalcdep.2013.04.007 [PubMed: 23647731]

Passie T, Emrich HM, Karst M, Brandt SD, & Halpern JH (2012). Mitigation of post-traumatic stress symptoms by cannabis resin: A review of the clinical and neurobiological evidence. Drug testing and Analysis, 4, 649–659. 10.1002/dta.1377 [PubMed: 22736575]

Persson A, Back SE, Killeen TK, Brady KT, Schwandt ML, Heilig M, & Magnusson Å (2017). Concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE): A pilot study in alcohol-dependent women. Journal of Addiction Medicine, 11, 119–125. doi: 10.1097/ADM.0000000000000286 [PubMed: 28079572]

Pizzimenti CL, Navis TM, & Lattal KM (2017). Persistent effects of acute stress on fear and drug-seeking in a novel model of the comorbidity between post-traumatic stress disorder and addiction. Learning & Memory, 24, 422–431. 10.1101/lm.044164.116 [PubMed: 28814468]

Roberts NP, Roberts PA, Jones N, & Bisson JI (2015). Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis. Clinical Psychology Review, 38, 25–38. https://doi.org/10.10167j.cpr.2015.02.007 [PubMed: 25792193]

Roy-Byrne PP, Stang P, Wittchen HU, Ustun B, Walters EE, & Kessler RC (2000). Lifetime panic–depression comorbidity in the National Comorbidity Survey: Association with symptoms, impairment, course and help-seeking. The British Journal of Psychiatry, 176, 229–235. 10.1192/bjp.176.3.229 [PubMed: 10755069]

Saladin ME, Drobes DJ, Coffey SF, Dansky BS, Brady KT, & Kilpatrick DG (2003). PTSD symptom severity as a predictor of cue-elicited drug craving in victims of violent crime. Addictive Behaviors, 28, 1611–1629. 10.1016/j.addbeh.2003.08.037 [PubMed: 14656549]

Special advisory committee on the epidemic of opioid overdoses. (2018) National report: Apparent opioid-related deaths in Canada (Jaunary 2016 to March 2018). Ottawa: Public Health Agency of Canada Accessed on December 3rd, 2018 Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/national-report-apparent-opioid-related-deaths-released-september-2018.html

Tull MT, Gratz KL, McDermott MJ, Bordieri MJ, Daughters SB, & Lejuez CW (2016). The role of emotion regulation difficulties in the relation between PTSD symptoms and the learned association between trauma-related and cocaine cues. Substance Use & Misuse, 51, 1318–1329. 10.3109/10826084.2016.1168445 [PubMed: 27224676]

Tupper KW, Wood E, Yensen R, & Johnson MW (2015). Psychedelic medicine: A re- emerging therapeutic paradigm. Canadian Medical Association Journal, 187, 1054–1059. 10.1503/cmaj.141124 [PubMed: 26350908]

Urban Health Research Institute. (2013). Drug situation in Vancouver. BC Centre for Excellence in HIV/AIDS Accessed on December 3rd, 2018: http://www.bccsu.ca/wp-content/uploads/2016/08/dsiv2013.pdf

Van Ameringen M, Mancini C, Patterson B, & Boyle MH (2008). Post-traumatic stress disorder in Canada. CNS Neuroscience & Therapeutics, 14, 171–181. 10.1111/j.1755-5949.2008.00049.x [PubMed: 18801110]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Weiss NH, Tull MT, Viana AG, Anestis MD, & Gratz KL (2012). Impulsive behaviors as an emotion regulation strategy: Examining associations between PTSD, emotion dysregulation, and impulsive behaviors among substance dependent inpatients. Journal of Anxiety Disorders, 26, 453–458. 10.1016/jjanxdis.2012.01.007 [PubMed: 22366447]

Wood E, Stoltz JA, Montaner JS, & Kerr T (2006). Evaluating methamphetamine use and risks of injection initiation among street youth: The ARYS study. Harm Reduction Journal, 3, 1–6. 10.1186/1477-7517-3-18 [PubMed: 16403229]

Young S, & Fairbairn N (2018). Expanding supervised injection facilities across Canada: Lessons from the Vancouver experience. Canadian Journal of Public Health, 109, 1–4. [PubMed: 29981074]

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Table 1

Characteristics of people who use illicit drugs in Vancouver, Canada, stratified by non-fatal drug overdose (N = 1059)

Characteristic	Non-fatal drug overdose*		*p* - value
	Yes (%) n = 171	No (%) n = 888	
Provisional PTSD diagnosis			
Yes	94 (55.0)	320 (36.0)	<0.001
No	77 (45.0)	568 (64.0)	
Age			
Median split	64 (37.4)	466 (52.5)	<0.001
	107 (62.6)	422 (47.5)	
Gender			
Male	117 (68.4)	579 (65.2)	0.417
Non-male	54 (31.6)	309 (34.8)	
Ethnicity			
White	86 (50.3)	474 (53.4)	0.477
Non-White	84 (49.1)	411 (46.3)	
Homelessness *			
Yes	73 (42.7)	168 (18.9)	<0.001
No	96 (56.1)	717 (80.7)	
Incarceration *			
Yes	24 (14.0)	44 (5.0)	<0.001
No	146 (85.4)	842 (94.8)	
Public injection drug use *			
Yes	79 (46.2)	167 (18.8)	<0.001
No	92 (53.8)	718 (80.9)	
Needed help injecting drugs *			
Yes	53 (31.0)	110 (12.4)	<0.001
No	118 (69.0)	778 (87.6)	
Daily heroin injection *			
Yes	49 (28.7)	149 (16.8)	<0.001
No	122 (71.3)	739 (83.2)	
Daily stimulant injection *			
Yes	37 (21.6)	110 (12.4)	0.001
No	134 (78.4)	778 (87.6)	
Daily prescription opioid use *			
Yes	8 (4.7)	16 (1.8)	0.021
No	163 (95.3)	872 (98.2)	
Daily alcohol use *			

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Characteristic	Non-fatal drug overdose*		*p* - value
	Yes (%) n = 171	No (%) n = 888	
Yes	17 (9.9)	72 (8.1)	0.431
No	154 (90.1)	815 (91.8)	
Opioid agonist treatment*			
Yes	83 (48.5)	395 (44.5)	0.0303
No	87 (50.9)	492 (55.4)	

*Activities in the previous 6 months

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Table 2

Bivariate and multivariate logistic regression analysis of factors associated with non-fatal overdose among people who use illicit drugs in Vancouver, Canada (N = 1059)

Characteristic	Unadjusted		Adjusted	
	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value
Provisional PTSD diagnosis				
(yes vs. no)	2.17 (1.56 – 3.02)	<0.001	1.98 (1.41 – 2.79)	<0.001
Age				
(Median split)	0.54 (0.39 – 0.76)	<0.001	-	-
Gender				
(Male vs. non-male)	1.16 (0.81 – 1.64)	0.417	-	-
Ethnicity				
(White vs. non-white)	0.89 (0.64 – 1.23)	0.477	-	-
Homelessness *				
(yes vs. no)	3.25 (2.29 – 4.59)	<0.001	-	-
Incarceration *				
(yes vs. no)	3.15 (1.86 – 5.33)	<0.001	-	-
Public injection drug use *				
(yes vs. no)	3.69 (2.62 – 5.21)	<0.001	3.49 (2.46 – 4.94)	<0.001
Needed help injecting drugs *				
(yes vs. no)	3.18 (2.17 – 4.65)	<0.001	-	-
Daily heroin injection *				
(yes vs. no)	1.99 (1.37 – 2.90)	<0.001	-	-
Daily stimulant injection *				
(yes vs. no)	1.95 (1.29 – 2.96)	0.002	-	-
Daily prescription opioid use *				
(yes vs. no)	2.67 (1.13 – 6.35)	0.026	-	-
Daily alcohol use *				
(yes vs. no)	1.25 (0.72 – 2.18)	0.432	-	-
Opioid agonist treatment *				
(yes vs. no)	1.19 (0.86 – 1.65)	0.303	-	-

* Activities in the previous 6 months