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REVIEW

Prevalence and high-risk behaviors associated with non-fatal overdose among people who use illicit opioids: A systematic review and meta-analysis

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ABSTRACT

Background: The aim of the present study was to determine the prevalence of non-fatal overdose among people who use illicit opioids (PWUIOs) and determine the demographic and behavioral characteristics associated with non-fatal overdose among this population.

Methods: Studies in English published before February 1, 2021, were searched for on *PubMed, Scopus, Cochrane*, and *Web of Science* to identify primary studies on the factors associated with non-fatal overdose among PWUIOs. After reviewing for study duplicates, the full-texts of selected papers were assessed for eligibility using PICOs criteria.

Results: After a detailed assessment of over 13,845 papers, a total of 67 studies met the eligibility criteria. The findings showed a past-year pooled prevalence rate of non-fatal overdose among PWUIOs of 26% (95% CI, 23% −29%). Greater odds of non-fatal overdose among PWUIOs was associated with (i) being younger, (ii) being female, (iii) being homeless, (iv) individuals who received money, goods, or drugs in exchange for sex, (v) individuals who had witnessed somebody else have an overdose, (vi) individuals who had used public spaces as primary injection locations, (vii) individuals who reported polydrug use, (vii) use of non-injection methamphetamine, and (viii) high injecting frequency (more than two daily drug injections).

Conclusion: Harm-reduction programs should consider the provision of education concerning overdose-related risk factors to the vulnerable and hard-to-reach PWUIOs.

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Illicit opioid use; non-fatal overdose; non-injection methamphetamine; injecting frequency; meta-analysis

Introduction

Non-fatal overdose is one of the strongest predictors of fatal overdose (Caudarella et al., 2016b). It often leads to morbidities, including pulmonary diseases, physical injury, neuropathy, and hypoxic neural injury (Warner-Smith et al., 2002; Warner-Smith et al., 2001). It has been reported that approximately half of people who use illicit opioids (PWUIOs) have experienced at least one non-fatal overdose their lifetime (Mcgregor et al., 1998). Overdose occurs in approximately one-third of drug-related deaths among PWUIOs (Degenhardt et al., 2011; Saini et al., 2020). Studies have reported that more than two-thirds of drug users have been exposed to at least one non-fatal overdose during their life (Martins et al., 2015), with more than two million drug-related visits to

emergency department in the US during the early 2000s (Burns et al., 2004). As a result of this high baseline risk, countries worldwide, such as the North American community, are in danger of an overdose epidemic, now rooted in synthetic drugs (e.g., fentanyl and related analogs) (Ciccarone, 2019; Fischer et al., 2019).

PWUIOs are mostly at the highest risk of overdose. It appears that non-fatal overdose is considered as a risk factor for future fatal and non-fatal overdoses, and is associated with a diverse range of health risks, including muscular dysfunction and cognitive impairment, and has high healthcare expenses (Caudarella et al., 2016b; Warner-Smith et al., 2001). Polysubstance use, homelessness, injecting in public spaces, and confrontations with the police are other correlates of non-fatal overdose (Armoon et al., 2021; Bohnert et al., 2011; Britton, Wines, et al., 2010; Coffin et al., 2003; Darke et al., 2005). The World Health Organization (WHO) recommends providing opioid antagonists such as naloxone to people who are likely to experience overdose after substance use (Balster et al., 2016). Non-fatal overdose causes serious morbidity (Warner-Smith et al., 2001) and some studies have identified a history of non-fatal overdose experiences as a significant predictor of future overdoses (Kerr et al., 2007; Stoové et al., 2009). Risk factors associated with overdose from synthetic drugs primarily used to relieve pain (for example morphine) have been investigated, emphasizing the drug dose (Bohnert et al., 2016; Gwira Baumblatt et al., 2014) and the pharmacological characteristics of opioids (Roxburgh et al., 2019). Factors independently associated with experiencing a non-fatal overdose include concurrent use of opioids and sedatives, concurrent use of opioids and psychostimulants such as cocaine, housing problems, injection as the route of opioid administration, incarceration history, and recent experience of overdose (Armoon et al., 2021). Higher overdose rates have been associated with alcohol use among injecting drug users have in some studies (Kinner et al., 2012) and may represent pharmacological

or behavioral interactions between alcohol and injected substances (Heinze et al., 2002). Moreover, In a study among people who are injecting drug users (PWIDs) Grau et al. (2009) reported that about 50% of studied cases had experienced a non-fatal overdose in the year prior to the study (Grau et al., 2009). Overdose is much more prevalent after a period of drug abstinence, when tolerance is at the minimal level (e.g., following release from drug treatment programs or jail). Therefore, those who report a non-fatal overdose in the past are more likely to experience another (potentially fatal) overdose in the future (Powis et al., 1999).

Only a few meta-analyses have investigated the prevalence of non-fatal overdose among PWIDUs (Colledge et al., 2019). With non-fatal overdose increasing among PWUIOs(Saini et al., 2020). It is essential to improve the knowledge concerning this problem and its associated risk factors to inform overdose prevention and assistance programs. Therefore, the present study assessed the prevalence of non-fatal overdose among PWUIOs and aimed to identify the demographic and behavioral characteristics associated with non-fatal overdose among this population.

Methods

Search strategy and study selection

This study was conducted according to the Protocols of Systematic Reviews and Meta-Analyses (PRISMA) (Bayani et al., 2020; Rezaei et al., 2020). The study selection steps are outlined in Figure 1.

Fig 1. PRISMA flow diagram

The papers obtained in the search were published from January 1, 1995 to February 1, 2021. For inclusion in the present review, two independent researchers (AB and BA) reviewed four electronic databases (PubMed, Scopus, Web of Science, and the Cochrane Library), with the

following search keywords: (Death, Sudden, Cardiac [MeSH Terms]) or (Heart Arrest [MeSH Terms]) or (non-fatal overdose [Title/Abstract])) or (Death [MeSH Terms]) or (Fetal Death [MeSH Terms]) or (Myocardial Infarction [MeSH Terms]) or (difficulties with breathing [Title/Abstract]) or (convulsions [MeSH Terms]) or (Seizures [MeSH Terms]) or (inability to wake up [Title/Abstract]) or (collapsing [Title/Abstract]) or (blue skin color [Title/Abstract]) or (Unconsciousness [MeSH Terms]) and (Opium Dependence [MeSH Terms]) or (Morphine Dependence [MeSH Terms]) or (Drug Users [MeSH Terms]) or (Heroin [MeSH Terms]) or (Heroin Dependence [MeSH Terms]) or (Opioid-Related Disorders [MeSH Terms]) or (Opiate Overdose [MeSH Terms]). The formal search strategy is outlined in Table 1. Paper references were managed using EndNote X7 software (Thomson Reuters). The search strategy from the four databases including additional manual searches from the paper references, resulted in 13,845 papers.

Duplicate papers were excluded. First, two co-authors reviewed the paper titles and abstracts independently, based on population, intervention, comparison, outcome, and study design (PICOS) criteria. A third member of the research team (AMB) provided input as needed, and helped in solving disagreements about papers included in the study. Second, AB and BA analyzed the full papers retained, considering the study inclusion criteria based on PICO, and exclusion criteria such as no access to the full paper and/or missing key data. Only papers written in English were included in the study from January 1st, 1995 to February 1, 2021 and included in the World Health Organization (WHO) countries. Based on PICOS criteria, the other inclusion criteria were as follows. For the “population”, only PWUIOs were included; for the “intervention”, socio-demographical determinants (age, sex, housing status) and high-risk behaviors (e.g., receiving

money, goods, or drugs in exchange for sex), individuals who had witnessed somebody else have an overdose, individuals who had used public spaces as primary injection locations, PWUIOs who reported polydrug use, non-injection of methamphetamine, and injecting frequency in the past year) were looked for; the "comparison" group was PWUIOs who had not experienced any non-fatal overdose in the previous year; the "outcome" was having non-fatal overdose in the last year; the "study design" integrated cross-sectional, cohort or case-control studies. Qualitative studies, secondary studies which did not include primary data, systematic reviews, and meta-analysis studies were excluded. Papers with too significant heterogeneity or outcome variations from the study groups considered were also excluded. Papers or variables included in the studies retained that were not detailed enough to be included in the meta-analysis were also not considered as associated variables of non-fatal overdose among PWUIOs (i.e., concurrent sedative/hypnotic use, pharmacy shopping, overlapping prescriptions, and syringe reuse). A modified version of the Newcastle-Ottawa Scale (NOS) (Stang, 2010) was utilized to assess the quality of the reviewed papers and risk of bias in each study (Table 2).

Data extraction and study quality assessment

Two of the co-authors (AB and BA) reviewed and decided on paper inclusion using a standardized data gathering form. All the disagreements between the two researchers were eliminated by getting help from two other members of the research team (EA and RM). For the data extraction and management, *Microsoft Excel* software was used. Two independent reviewers (BA and AB) selected the papers in two phases. In the first phase, the duplicated titles/abstracts (89% agreement) according to the six criteria listed below (1-6) were deleted. In the second phase, titles/abstracts

that met the inclusion criteria were chosen for full-text review according to the inclusion criteria (96% agreement).

The data extracted included the surname of the first author, publication date, participant demographic data (age, sex, being homeless), and other features such as type of high-risk behaviors such as (i) individuals who received money, goods, or drugs in exchange for sex, (ii) individuals who had witnessed somebody else have an overdose, (iii) individuals who had used public spaces as primary injection locations(iv) individuals who reported polydrug use, (v) use of non-injection methamphetamine, and (vi) injecting frequency.

Table 2. Quality of studies and risk of bias assessment using Newcastle-Ottawa Scale.

The Newcastle-Ottawa Scale (NOS; (Stang, 2010) was used to determine the methodological quality of studies included (sample representativeness or size, methodology). A maximum of five quality scores were defined for items. Publications with a total score of 0-2, 3, 4 and 5 points were recorded as “unsatisfactory”, “satisfactory”, “good” or “very good” respectively. The agreement beyond chance (unweighted kappa) was used to assess the agreement between the two authors (BA and AB) during the quality evaluation. The levels of poor, slight, fair, moderate, substantial, and almost perfect levels of agreement were demonstrated by the values 0, 01–0.02, 0.021–0.04, 0.041–0.06, 0.061–0.08, and 0.081–1.00, respectively (Landis et al., 1977).

Data synthesis and statistical analysis

The present study was conducted by creating pooled odds ratios (ORs) and 95% confidence intervals (Cis) for identifying factors associated to non-fatal overdose. The OR was computed applying a 2*2 table, and an OR<1 was considered as a positive association between non-fatal overdose and the target variable. An OR>1 (as the statistical threshold for assessing the association between outcome variables and expositive variables) represents a strong association between variables and vice versa. To assess the lack of correlation among studies, the Q test with a *p*-value <0.05 and I^2 statistics with a cutoff of ≥50% were considered. A CI of 95% was considered for I^2 where the negative values were assumed as zero. The random-effects model was used to gain the pooled estimation, considering the different sampling methods of the studies. To recognize publication biases both in graphical and statistical aspects, Egger's publication bias methods were used. A *p*-value of less than 0.05 was considered significant. The association between high-risk behaviors was shown by an OR and 95% CI, and the results were visualized in forest plots. In the analysis phase, R 3.5.1 with the "meta" package was used to conduct the meta-analysis.

Results

Study characteristics

After the rigorous search process, 67 studies were identified for inclusion in the meta-analysis (Bazazi et al., 2015; Bergenstrom et al., 2008; Blackburn et al., 2017; Bonar et al., 2016; Bretteville-Jensen et al., 2015; Britton, Wines Jr, et al., 2010; Brugal et al., 2002; Brugal et al., 2005; Burke et al., 2020; Caudarella et al., 2016a; Cheng et al., 2020; Cochran et al., 2017; Coffin et al., 2007; Darke et al., 1997; Darke et al., 2005; Darke et al., 2007; Dayton et al., 2020; Escudero et al., 2016; Fairbairn et al., 2008; Fairgrieve et al., 2020; Fendrich et al., 2019; Finkelstein et al., 2016; Fischer et al., 2004; Galea et al., 2006; Groenewald et al., 2019; Grzebinski et al., 2020;

Hakansson et al., 2008; Hunter et al., 2018; Kerr et al., 2007; Kilaru et al., 2020; Kinner et al., 2012; Lagu et al., 2006; Lake et al., 2015; Latkin et al., 2018; Lowder et al., 2020; Madah-Amiri et al., 2019; Martin et al., 2014; Mcgregor et al., 1998; Milloy et al., 2010; Nam et al., 2020; Noroozi, Higgs, et al., 2020; O'Keefe et al., 2018; O'Halloran et al., 2017; Ochoa et al., 2005; Otachi et al., 2020; Park et al., 2018; Pizzicato et al., 2020; Prangnell et al., 2019; Rafful et al., 2018; Riggs et al., 2020; Saleem et al., 2020; Schiavon et al., 2018; Seal et al., 2001; Sherman et al., 2007; Stewart et al., 2002; Suffoletto et al., 2020; Tobin et al., 2003; Trayner et al., 2020; Uusküla et al., 2015; van Beek et al., 2004; Wallace et al., 2019; Walley et al., 2014; Yang et al., 2015; Yin et al., 2007; Yule et al., 2019; Yule et al., 2018; Zhou et al., 2016). The selected studies were from six WHO regions (43 from the Region of the Americas [n=4,172,478 participants], 10 from the European Region [n=24,053 participants], one from South-East Asia Region [n=252 participants], 11 from the Western Pacific Region [n=8,562 participants], one from the African Region [n=200 participants], and one from Eastern Mediterranean Region [n=564 participants]. The USA had the highest number of studies (n=29, 4,055,985 participants). Considering country income level, 56 studies were conducted within high-income countries (n= 4,202,153), seven studies within upper-middle-income countries (n= 3,213), and three studies were from lower middle-income countries (n= 1,702).

Results of the meta-analysis

In Tables 3 and 4, the key characteristics of the included studies for high-risk behaviors associated with non-fatal overdose among PWUIOs are presented (Tables 3 and 4). Figure 2 shows the pooled prevalence rate of non-fatal overdose among PWUIOs to be 26% (95% CI, 23% -29%).

Table 3. Characteristics of non-fatal overdose among PWUIOs.

Figure 2. The prevalence of non-fatal overdose among PWUIOs.

Socio-demographical for non-fatal overdose

Table 5 shows there was a significant association between age<30 years with non-fatal overdose among PWUIOs compared with those aged >30 years (OR=1.31, 95%CI=1.16-1.48). (Table 5). Table 5 also shows there was an association between being female and non-fatal overdose among PWUIOs. The findings show that PWUIOs who were female were 1.66 times more likely to report having had a non-fatal overdose during past year compared with males (OR=1.66, 95%CI=1.01-2.73). Additionally, Table 5 shows there was a positive relationship between being homeless and non-fatal overdose among PWUIOs. Participants who were homeless were 1.64 times more likely to have had a non-fatal overdose in the past 12 months compared with those not homeless (OR = 1.64, 95%CI = 1.45- 1.84).

High-risk behavior for non-fatal overdose

Findings indicate there was an association between receiving money, goods, or drugs in exchange for sex non-fatal overdose among PWUIOs (Table 5). The findings showed that PWUIOs who received money, goods, or drugs in exchange for sex were 1.77 times more likely to report having had a non-fatal overdose during last year compared with those that did not (OR=1.77, 95%CI=1.46-2.15). There were no significant associations found between those who had used a speedball and non-fatal overdose among PWUIOs (OR=1.33, 95% CI=0.85-2.08) (Table 5). There was also a positive association between those who had witnessed an overdose and non-fatal overdose among PWUIOs. Individuals who had witnessed an overdose were 2.22 times more

likely to have had a non-fatal overdose (past 12 months) compared with those who had not (OR=2.22, 95%CI=1.61-3.08) (Table 5).

Findings indicate that there was an association between public injecting and non-fatal overdose among PWUIOs. PWUIOs who had injected in public were 1.61 times more likely to report having had a non-fatal overdose during past year compared with those who had not (OR=1.61, %CI=1.37-1.89) (Table 5). There was also an association between polydrug use (>2 types of illicit drug use) and non-fatal overdose among PWUIOs. PWUIOs who reported polydrug use were 1.73 times more likely to report having had a non-fatal overdose among PWUIOs during past year compared with individuals using a single drug (OR=1.73, 95%CI=1.44-2.07) (Table 5).

There was a positive relationship between non-injection methamphetamine use and non-fatal overdose among PWUIOs. PWUIOs who used non-injected methamphetamine were 2.01 times more likely to have had a non-fatal overdose among PWUIOs in the last 12 months (OR = 2.01, 95%CI = 1.66- 2.43). (Table 5). There was also a significant association between injecting frequency and non-fatal overdose among PWUIOs. PWUIOs who had a high injecting frequency (more than two times daily) were 2.66 times more likely to have had non-fatal overdose in the previous 12 months than PWUIOs who did not report such an injecting frequency (OR=2.66, 95%CI=1.80-3.92) (Table 5).

To identify probable publication bias, the Egger's test was performed. The publication bias test indicates considerable bias based on Egger's test (coefficient = 3.66, $p<0.001$). Therefore, met-trim analysis was performed in order to remove the effect of publication bias on the pooled OR. The meta-trim analysis indicated that the pooled OR was 0.14 (95% CI, 0.11–0.25) in the random effect model.

Discussion

The present study assessed the prevalence of non-fatal overdose among PWUIOs and attempted to identify the demographic and behavioral characteristics associated with non-fatal overdose among this population. The findings indicated that greater odds of non-fatal overdose among PWUIOs was associated with (i) being of younger age, (ii) being female, (iii) being homeless, (iv) individuals who received money, goods, or drugs in exchange for sex, (v) individuals who had witnessed somebody else have an overdose, (vi) individuals who had used public spaces as primary injection locations, (vii) individuals who reported polydrug use, (vii) individuals who had used non-injection methamphetamine, and (viii) high injecting frequency (more than two times daily).

The present review is the first to quantify the prevalence rate of non-fatal overdose among PWUIOs. It also identified various high-risk behaviors associated with the prevalence patterns (epidemiology) among PWUIOs and included data from six WHO regions. A recent review reported that approximately 3.2 million drug consumers in the past 12 months as having a non-fatal overdose worldwide (Colledge et al., 2019). Such patterns of prevalence are in line with those of a prior systematic review on fatal and non-fatal overdose in drug users (Martins et al., 2015). According to that previous study, the range of recent non-fatal overdose varied from 6.7% to 32.7% among PWIDUs (compared to 20.5% in the present study; 95% CI 15.0–26.1%). Additionally, they reported a range of 29.0%-59.0% concerning lifetime non-fatal overdose (compared to 41.5% in the present study; 95% CI: 34.6–48.4%).

Findings showed that PWUIOs who were female were more likely to experience non-fatal overdose. According to previous studies, high rates of overdose among women have been reported, with 37.5% reporting a lifetime overdose and 18% reporting an overdose in the past three months,

with most overdoses related to heroin or nonmedical use of prescription opioids (El-Bassel et al., 2020; Goldenberg, 2020). Although opioid-related overdoses is a major public health problem and may affect many groups of individuals, current knowledge of gendered experiences and requirements in the context of drug overdoses are arguably inadequate (Collins et al., 2019). To respond to this issue, gender-based experiences must be investigated, including the unique harm-reduction and addiction service requirements of women who use drugs (Azim et al., 2015; Strathdee et al., 2015). For example, harm-reduction services are more male-oriented, and females often indicate highly gendered barriers to accessing harm-reduction, such as overlapping stigmas, concerns related to safety, and the threat of violence in service delivery environments (Boyd et al., 2018).

According to the literature, an experience of an overdose in the past year was significantly related to using any type of illicit substances before 30 years of age among PWIDUs. The research findings here are in line with other study reporting that opioid users who were younger were more likely to report overdose (Nguyen et al., 2020). The onset age of opioid use is also an essential risk factor, given that earlier research has reported a consistent association between younger onset of substance use and higher susceptibility to substance dependence, leading to further health and social-related problems (Baldwin et al., 2013; Bazrafshan et al., 2019; Ghiasvand et al., 2018; King et al., 2007; Noroozi, Farhadi, et al., 2020). Non-fatal overdoses could be attributed to the association between a greater susceptibility to non-fatal overdose and less experience in injecting drugs, as well as a lower level of tolerance. However, these data were inconsistent with some international investigations, reporting a correlation between a longer-term history of injection and a recent overdose event (Darke et al., 2003). Previous studies have also demonstrated an association between encountering non-fatal overdose and polysubstance use in the past six months

among PWIDUs. This finding is also supported by other research, suggesting a strong correlation between fatal and non-fatal overdose and polydrug use (Darke et al., 2003; Hakkarainen et al., 2019). It is worth noting that polysubstance users also encounter more complex issues, such as homelessness and greater exposure to violence (Bazazi et al., 2011).

There was an independent and strong relationship between homelessness and overdose, in line with the data presented in previous research (Fischer et al., 2004). The finding has been attributed to the higher intensity of substance use among homeless populations (Fischer et al., 2004). Other researchers have addressed homelessness as the determining factor in poor health status among PWIDUs (Galea et al., 2002). Additionally, rushed injection attempts in public may increase overdose risk in this group (Broadhead et al., 2002; Dovey et al., 2001). Such an explanation could also be attributed to the relationship between overdose and using drugs in public identified in the present study. Rushed injections among homeless individuals may be due to avoiding police confrontations. Individuals might also administer too many psychoactive substances leading to overdoses (Brugal et al., 2002).

Witnessing others' overdose has been reported as a key risk factor for self-overdose in prior research. Such experience (witnessing overdose) is highly prevalent in young PWIDUs (Ochoa et al., 2005).The findings suggested that the likelihood of experiencing a recent overdose experience was greater among those using methamphetamine, and in line with the results of some other empirical studies (Gossop et al., 2002; Kinner et al., 2012). In the present study, there were associations between non-fatal overdose and non-injection methamphetamine use among PWIDUs as has been reported in several studies (Coffin et al., 2003; Sergeev et al., 2003). There were also associations in the present study between overdose and opiates, alcohol, and benzodiazepines use among PWIDs as has been reported in several studies (Coffin et al., 2003; Sergeev et al., 2003).

Such drugs are depressants of the central nervous system, therefore, the risk of overdose is increased following their use, in particular when consumed in combination with other psychoactive substances. Prior findings have indicated an association between a significantly-declined risk of overdose and non-injection use of any illicit substance (Brugal et al., 2002; Darke et al., 2003).

A study (Fairbairn et al., 2008) suggested a correlation between increased overdose events and experiencing transactional sex. Individuals who report such behaviors could be classified into a vulnerable subgroup, reflecting the chaotic or unsafe use of substances associated with enhanced sexual risks. Such data also signify the need for providing proper care services by doctors specializing in sexually dysfunctional behavior. The relationship between sexual activity and overdose requires further investigation.

Limitations and strengths of the present study

One of the limitations of the present study was related to the fact that all the studies reviewed were based on self-report data which is subject to well-known methods biases (e.g., memory recall, social desirability, etc.). Also, most of the selected studies comprised cross-sectional designs, meaning causal and temporal relationships between risk behavior and non-fatal overdose were not possible. One of the key strengths of the present review was that it examined many different variables and high-risk variables associated with non-fatal overdose. Also, the comprehensive search strategy, the use of major databases, and the relatively large number of studies that met the inclusion criteria are major strengths. Additionally, every observational study was evaluated, regardless of geographical location or date of publication. Overall, 13,845 papers were initially reviewed, and 67 studies that met the inclusion criteria were considered.

Conclusion

The present study's results indicate that a significant proportion of the PWUIOs in the studies evaluated experienced non-fatal overdoses. The characteristics with the strongest association with non-fatal overdose were being of younger age, being female, being homeless, individuals who received money, goods, or drugs in exchange for sex, individuals who had witnessed using public spaces as primary injection locations, individuals who reported poly-drug use, non-injection methamphetamine use, and a high injecting frequency. Consequently, harm-reduction programs should consider the provision of education concerning overdose-related risk factors to the vulnerable and hard-to-reach PWUIOs. The findings of the present meta-analysis may improve harm reduction strategies for drug users and help improve the requirements of enforcement-based responses to illicit drug use within health-related programs.

Abbreviations

People who use illicit opioids (PWUIOs)

Confidence intervals (CIs)

Newcastle-Ottawa Scale (NOS)

Odds ratio (OR)

Population, Intervention, Comparator, Outcomes (PICO)

Protocols of Systematic Reviews and Meta-Analyses (PRISMA)

PWIDUs: people who are injecting drug users.

World Health Organization (WHO)

References

Armoon, B., SoleimanvandiAzar, N., Rostami, M., Higgs, P., Bayani, A., Bayat, A.-H., Mohammadi, R., Ahounbar, E., & Fattah Moghaddam, L. (2021). Drug type and risk behaviors associated with non-fatal overdose among people who use drugs: a systematic review and meta-analysis. *Journal of Addictive Diseases*, 1-12. doi: https://doi.org/10.1080/10550887.2021.1950262

Azim, T., Bontell, I., & Strathdee, S. A. (2015). Women, drugs and HIV. *International Journal of Drug Policy, 26*, S16-S21.

Baldwin, P., Shrestha, R., Potrepka, J., & Copenhaver, M. (2013). The age of initiation of drug use and sexual behavior may influence subsequent HIV risk behavior: a systematic review. *International Scholarly Research Notices, 976035*(doi: 10.1155/2013/976035).

Balster, R. L., & Walsh, S. L. (2016). Ensure global access to naloxone for opioid overdose management. *Addiction, 111*(4), 589-590. doi: 10.1111/add.13274

Bayani, A., Ghiasvand, H., Rezaei, O., Fattah Moghaddam, L., Noroozi, A., Ahounbar, E., Higgs, P., & Armoon, B. (2020). Factors associated with HIV testing among people who inject drugs: a meta-analysis. *Journal of Addictive Diseases*, 1-14. doi: 10.1080/10550887.2020.1771235

Bazazi, A. R., Yokell, M., Fu, J. J., Rich, J. D., & Zaller, N. D. (2011). Illicit use of buprenorphine/naloxone among injecting and noninjecting opioid users. *Journal of Addiction Medicine, 5*(3), 175.

Bazazi, A. R., Zelenev, A., Fu, J. J., Yee, I., Kamarulzaman, A., & Altice, F. L. (2015). High prevalence of non-fatal overdose among people who inject drugs in Malaysia: Correlates

of overdose and implications for overdose prevention from a cross-sectional study. *International Journal of Drug Policy, 26*(7), 675-681.

Bazrafshan, M. R., Noroozi, M., Ghisvand, H., Noroozi, A., Alibeigi, N., Abbasi, M., Higgs, P., & Armoon, B. (2019). Comparing injecting risk behaviors of long-term injectors with new injectors in Tehran, Iran. *Substance Use & Misuse, 54*(2), 185-190.

Bergenstrom, A., Quan, V. M., Nam, L. V., Mcclausland, K., Thuoc, N. P., Celentano, D., & Go, V. (2008). A cross-sectional study on prevalence of non-fatal drug overdose and associated risk characteristics among out-of-treatment injecting drug users in North Vietnam. *Substance Use & Misuse, 43*(1), 73-84.

Blackburn, N., Lancaster, K., Ha, T., Latkin, C., Miller, W., Frangakis, C., Chu, V., Sripaipan, T., Quan, V., & Minh, N. (2017). Characteristics of persons who inject drugs and who witness opioid overdoses in Vietnam: a cross-sectional analysis to inform future overdose prevention programs. *Harm Reduction Journal, 14*(1), 1-9.

Bohnert, A. S., Logan, J. E., Ganoczy, D., & Dowell, D. (2016). A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with Chronic pain. *Medical Care, 54*(5), 435-441. doi: 10.1097/mlr.0000000000000505

Bohnert, A. S., Nandi, A., Tracy, M., Cerdá, M., Tardiff, K. J., Vlahov, D., & Galea, S. (2011). Policing and risk of overdose mortality in urban neighborhoods. *Drug and Alcohol Dependence, 113*(1), 62-68. doi: 10.1016/j.drugalcdep.2010.07.008

Bonar, E. E., & Bohnert, A. S. (2016). Perceived severity of and susceptibility to overdose among injection drug users: relationships with overdose history. *Substance Use & Misuse, 51*(10), 1379-1383.

Boyd, J., Collins, A. B., Mayer, S., Maher, L., Kerr, T., & McNeil, R. (2018). Gendered violence and overdose prevention sites: a rapid ethnographic study during an overdose epidemic in Vancouver, Canada. *Addiction, 113*(12), 2261-2270.

Bretteville-Jensen, A. L., Lillehagen, M., Gjersing, L., & Andreas, J. B. (2015). Illicit use of opioid substitution drugs: prevalence, user characteristics, and the association with non-fatal overdoses. *Drug and Alcohol Dependence, 147*, 89-96.

Britton, P. C., Wines, J. D., Jr., & Conner, K. R. (2010). Non-fatal overdose in the 12 months following treatment for substance use disorders. *Drug and Alcohol Dependence, 107*(1), 51-55. doi: 10.1016/j.drugalcdep.2009.09.005

Britton, P. C., Wines Jr, J. D., & Conner, K. R. (2010). Non-fatal overdose in the 12 months following treatment for substance use disorders. *Drug and Alcohol Dependence, 107*(1), 51-55.

Broadhead, R. S., Kerr, T. H., Grund, J.-P. C., & Altice, F. L. (2002). Safer injection facilities in North America: their place in public policy and health initiatives. *Journal of Drug Issues, 32*(1), 329-355.

Brugal, M. T., Barrio, G., Fuente, L. D. L., Regidor, E., Royuela, L., & Suelves, J. M. (2002). Factors associated with non-fatal heroin overdose: Assessing the effect of frequency and route of heroin administration. *Addiction, 97*(3), 319-327.

Brugal, M. T., Domingo-Salvany, A., Puig, R., Barrio, G., Garcia de Olalla, P., & De La Fuente, L. (2005). Evaluating the impact of methadone maintenance programmes on mortality due to overdose and aids in a cohort of heroin users in Spain. *Addiction, 100*(7), 981-989.

Burke, L. G., Zhou, X., Boyle, K. L., Orav, E. J., Bernson, D., Hood, M. E., Land, T., Bharel, M., & Frakt, A. B. (2020). Trends in opioid use disorder and overdose among opioid-

naive individuals receiving an opioid prescription in Massachusetts from 2011 to 2014. *Addiction, 115*(3), 493-504.

Burns, B. J., Phillips, S. D., Wagner, H. R., Barth, R. P., Kolko, D. J., Campbell, Y., & Landsverk, J. (2004). Mental health need and access to mental health services by youths involved with child welfare: A national survey. *Journal of the American Academy of Child & Adolescent Psychiatry, 43*(8), 960-970.

Caudarella, A., Dong, H., Milloy, M., Kerr, T., Wood, E., & Hayashi, K. (2016a). Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. *Drug and Alcohol Dependence, 162*, 51-55.

Caudarella, A., Dong, H., Milloy, M. J., Kerr, T., Wood, E., & Hayashi, K. (2016b). Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. *Drug and Alcohol Dependence, 162*, 51-55. doi: 10.1016/j.drugalcdep.2016.02.024

Cheng, T., Small, W., Nosova, E., Hogg, R., Hayashi, K., Kerr, T., & DeBeck, K. (2020). Overdose Risk and Acquiring Opioids for Nonmedical Use Exclusively from Physicians in Vancouver, Canada. *Substance Use & Misuse, 55*(12), 1912-1918.

Ciccarone, D. (2019). The triple wave epidemic: Supply and demand drivers of the US opioid overdose crisis. *International Journal of Drug Policy, 71*, 183-188. doi: 10.1016/j.drugpo.2019.01.010

Cochran, G., Gordon, A. J., Gellad, W. F., Chang, C.-C. H., Lo-Ciganic, W.-H., Lobo, C., Cole, E., Frazier, W., Zheng, P., & Kelley, D. (2017). Medicaid prior authorization and opioid medication abuse and overdose. *American Journal of Managed Care, 23*(5), e164.

Coffin, P. O., Galea, S., Ahern, J., Leon, A. C., Vlahov, D., & Tardiff, K. (2003). Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990-98. *Addiction, 98*(6), 739-747. doi: 10.1046/j.1360-0443.2003.00376.x

Coffin, P. O., Tracy, M., Bucciarelli, A., Ompad, D., Vlahov, D., & Galea, S. (2007). Identifying injection drug users at risk of nonfatal overdose. *Academic Emergency Medicine, 14*(7), 616-623.

Colledge, S., Peacock, A., Leung, J., Larney, S., Grebely, J., Hickman, M., Cunningham, E., Trickey, A., Stone, J., Vickerman, P., & Degenhardt, L. (2019). The prevalence of non-fatal overdose among people who inject drugs: A multi-stage systematic review and meta-analysis. *International Journal of Drug Policy, 73*, 172-184. doi: https://doi.org/10.1016/j.drugpo.2019.07.030

Collins, A. B., Boyd, J., Cooper, H. L., & McNeil, R. (2019). The intersectional risk environment of people who use drugs. *Social Science & Medicine, 234*, 112384.

Darke, S., & Hall, W. (2003). Heroin overdose: research and evidence-based intervention. *Journal of Urban Health, 80*(2), 189-200.

Darke, S., & Ross, J. (1997). Overdose risk perceptions and behaviours among heroin users in Sydney, Australia. *European Addiction Research, 3*(2), 87-92.

Darke, S., Williamson, A., Ross, J., Mills, K. L., Havard, A., & Teesson, M. (2007). Patterns of nonfatal heroin overdose over a 3-year period: Findings from the Australian treatment outcome study. *Journal of Urban Health, 84*(2), 283-291.

Darke, S., Williamson, A., Ross, J., & Teesson, M. (2005). Non-fatal heroin overdose, treatment exposure and client characteristics: Findings from the Australian treatment outcome study (ATOS). *Drug and Alcohol Review, 24*(5), 425-432. doi: 10.1080/09595230500286005

Dayton, L., Tobin, K., Falade-Nwulia, O., Davey-Rothwell, M., Al-Tayyib, A., Saleem, H., & Latkin, C. (2020). Racial disparities in overdose prevention among people who inject drugs. *Journal of Urban Health, 97*, 823-830.

Degenhardt, L., Bucello, C., Mathers, B., Briegleb, C., Ali, H., Hickman, M., & McLaren, J. (2011). Mortality among regular or dependent users of heroin and other opioids: A systematic review and meta-analysis of cohort studies. *Addiction, 106*(1), 32-51.

Dovey, K., Fitzgerald, J., & Choi, Y. (2001). Safety becomes danger: Dilemmas of drug-use in public space. *Health & Place, 7*(4), 319-331.

El-Bassel, N., Norcini Pala, A., Mukherjee, T. I., McCrimmon, T., Mergenova, G., Terlikbayeva, A., Primbetova, S., & Witte, S. S. (2020). Association of violence against female sex workers who use drugs with nonfatal drug overdose in Kazakhstan. *JAMA Network Open, 3*(10), e2020802-e2020802. doi: 10.1001/jamanetworkopen.2020.20802

Escudero, D. J., Marshall, B. D., Kerr, T., Hayashi, K., Feng, C., Guillemi, S. A., Hogg, R. S., Montaner, J., Wood, E., & Milloy, M.-J. (2016). No association between HIV status and risk of non-fatal overdose among people who inject drugs in Vancouver, Canada. *Addictive Behaviors, 60*, 8-12.

Fairbairn, N., Wood, E., Stoltz, J.-a., Li, K., Montaner, J., & Kerr, T. (2008). Crystal methamphetamine use associated with non-fatal overdose among a cohort of injection drug users in Vancouver. *Public Health, 122*(1), 70-78.

Fairgrieve, C., Nosova, E., Milloy, M., Fairbairn, N., DeBeck, K., Ahamad, K., Wood, E., Kerr, T., & Hayashi, K. (2020). Temporal changes in non-fatal opioid overdose patterns among people who use drugs in a Canadian setting. *Substance Abuse, 41*(3), 323-330.

Fendrich, M., Becker, J., & Hernandez-Meier, J. (2019). Psychiatric symptoms and recent overdose among people who use heroin or other opioids: Results from a secondary analysis of an intervention study. *Addictive Behaviors Reports, 10*, 100212.

Finkelstein, Y., Macdonald, E. M., Hollands, S., Sivilotti, M. L., Hutson, J. R., Mamdani, M. M., Koren, G., Juurlink, D. N., Safety, C. D., & Network, E. R. (2016). Repetition of intentional drug overdose: a population-based study. *Clinical Toxicology, 54*(7), 585-589.

Fischer, B., Brissette, S., Brochu, S., Bruneau, J., El-Guebaly, N., Noël, L., Rehm, J., Tyndall, M., Wild, C., & Mun, P. (2004). Determinants of overdose incidents among illicit opioid users in 5 Canadian cities. *CMAJ, 171*(3), 235-239.

Fischer, B., Pang, M., & Tyndall, M. (2019). The opioid death crisis in Canada: Crucial lessons for public health. *Lancet Public Health, 4*(2), e81-e82. doi: 10.1016/s2468-2667(18)30232-9

Galea, S., Nandi, A., Coffin, P. O., Tracy, M., Piper, T. M., Ompad, D., & Vlahov, D. (2006). Heroin and cocaine dependence and the risk of accidental non-fatal drug overdose. *Journal of Addictive Diseases, 25*(3), 79-87.

Galea, S., & Vlahov, D. (2002). Social determinants and the health of drug users: socioeconomic status, homelessness, and incarceration. *Public Health reports, 117*(Suppl 1), S135.

Ghiasvand, H., Bayani, A., Noroozi, A., Marshall, B. D., Koohestani, H. R., Hemmat, M., Mirzaee, M. S., Bayat, A. H., Noroozi, M., & Ahounbar, E. (2018). Comparing injecting and sexual risk behaviors of long-term injectors with new injectors: A meta-analysis. *Journal of Addictive Diseases, 37*(3-4), 233-244.

Goldenberg, S. M. (2020). Addressing violence and overdose among women who use drugs—Need for structural interventions. *JAMA network open, 3*(10), e2021066-e2021066. doi: 10.1001/jamanetworkopen.2020.21066

Gossop, M., Stewart, D., Treacy, S., & Marsden, J. (2002). A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. *Addiction, 97*(1), 39-47.

Grau, L. E., Green, T. C., Torban, M., Blinnikova, K., Krupitsky, E., Ilyuk, R., Kozlov, A. P., & Heimer, R. (2009). Psychosocial and contextual correlates of opioid overdose risk among drug users in St. Petersburg, Russia. *Harm Reduction Journal, 6*, 17. doi: 10.1186/1477-7517-6-17

Groenewald, C. B., Zhou, C., Palermo, T. M., & Van Cleve, W. C. (2019). Associations between opioid prescribing patterns and overdose among privately insured adolescents. *Pediatrics, 144*(5).

Grzebinski, S., Stein, L., & Dhamoon, M. S. (2020). Characteristics and outcomes of hospitalizations and readmissions for opioid dependence and overdose: nationally representative data. *Substance Abuse*, 1-8. doi: doi: 10.1080/08897077.2020.1823548

Gwira Baumblatt, J. A., Wiedeman, C., Dunn, J. R., Schaffner, W., Paulozzi, L. J., & Jones, T. F. (2014). High-risk use by patients prescribed opioids for pain and its role in overdose deaths. *JAMA Internal Medicine, 174*(5), 796-801. doi: 10.1001/jamainternmed.2013.12711

Hakansson, A., Schlyter, F., & Berglund, M. (2008). Factors associated with history of non-fatal overdose among opioid users in the Swedish criminal justice system. *Drug and Alcohol Dependence, 94*(1-3), 48-55.

Hakkarainen, P., O'Gorman, A., Lamy, F., & Kataja, K. (2019). (Re) conceptualizing "Polydrug use": capturing the complexity of combining substances. *Contemporary Drug Problems, 46*(4), 400-417.

Heinze, G., & Schemper, M. (2002). A solution to the problem of separation in logistic regression. *Statistics in Medicine, 21*(16), 2409-2419. doi: 10.1002/sim.1047

Hunter, K., Park, J. N., Allen, S. T., Chaulk, P., Frost, T., Weir, B. W., & Sherman, S. G. (2018). Safe and unsafe spaces: Non-fatal overdose, arrest, and receptive syringe sharing among people who inject drugs in public and semi-public spaces in Baltimore City. *International Journal of Drug Policy, 57*, 25-31.

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*(1), 39-45. doi: 10.1016/j.drugalcdep.2006.07.009

Kilaru, A. S., Xiong, A., Lowenstein, M., Meisel, Z. F., Perrone, J., Khatri, U., Mitra, N., & Delgado, M. K. (2020). Incidence of treatment for opioid use disorder following nonfatal overdose in commercially insured patients. *JAMA Network Open, 3*(5), e205852-e205852.

King, K. M., & Chassin, L. (2007). A prospective study of the effects of age of initiation of alcohol and drug use on young adult substance dependence. *Journal of Studies on Alcohol and Drugs, 68*(2), 256-265.

Kinner, S. A., Milloy, M., Wood, E., Qi, J., Zhang, R., & Kerr, T. (2012). Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. *Addictive Behaviors, 37*(6), 691-696.

Lagu, T., Anderson, B. J., & Stein, M. (2006). Overdoses among friends: drug users are willing to administer naloxone to others. *Journal of Substance Abuse Treatment, 30*(2), 129-133.

Lake, S., Hayashi, K., Buxton, J., Milloy, M.-J., Dong, H., Wood, E., Montaner, J., & Kerr, T. (2015). The effect of prescription opioid injection on the risk of non-fatal overdose among people who inject drugs. *Drug and Alcohol Dependence, 156*, 297-303.

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics*, 159-174.

Latkin, C. A., Edwards, C., Davey-Rothwell, M. A., Yang, C., & Tobin, K. E. (2018). The relationship between drug use settings, roles in the drug economy, and witnessing a drug overdose in Baltimore, Maryland. *Substance Abuse, 39*(3), 384-389.

Lowder, E. M., Amlung, J., & Ray, B. R. (2020). Individual and county-level variation in outcomes following non-fatal opioid-involved overdose. *Journal of Epidemiology and Community Health, 74*(4), 369-376.

Madah-Amiri, D., Skulberg, A. K., Braarud, A. C., Dale, O., Heyerdahl, F., Lobmaier, P., & Clausen, T. (2019). Ambulance-attended opioid overdoses: An examination into overdose locations and the role of a safe injection facility. *Substance Abuse, 40*(3), 383-388. doi: 10.1080/08897077.2018.1485130

Martin, G., Vallance, K., Macdonald, S., Stockwell, T., Ivsins, A., Chow, C., Michelow, W., & Duff, C. (2014). Nonfatal overdose from alcohol and/or drugs among a sample of recreational drug users. *Journal of Substance Use, 19*(3), 239-244. doi: 10.3109/14659891.2013.784369

Martins, S. S., Sampson, L., Cerdá, M., & Galea, S. (2015). Worldwide prevalence and trends in unintentional drug overdose: a systematic review of the literature. *American Journal of Public Health, 105*(11), e29-e49.

Mcgregor, C., Darke, S., Ali, R., & Christie, P. (1998). Experience of non-fatal overdose among heroin users in Adelaide, Australia: circumstances and risk perceptions. *Addiction, 93*(5), 701-711.

Milloy, M., Fairbairn, N., Hayashi, K., Suwannawong, P., Kaplan, K., Wood, E., & Kerr, T. (2010). Overdose experiences among injection drug users in Bangkok, Thailand. *Harm Reduction Journal, 7*(1), 1-7.

Nam, Y. H., Bilker, W. B., DeMayo, F. J., Neuman, M. D., & Hennessy, S. (2020). Incidence rates of and risk factors for opioid overdose in new users of prescription opioids among US Medicaid enrollees: A cohort study. *Pharmacoepidemiology and Drug Safety, 29*(8), 931-938.

Nguyen, A. P., Glanz, J. M., Narwaney, K. J., & Binswanger, I. A. (2020). Association of opioids prescribed to family members with opioid overdose among adolescents and young adults. *JAMA Network Open, 3*(3), e201018-e201018. doi: 10.1001/jamanetworkopen.2020.1018

Noroozi, M., Farhadi, M. H., Armoon, B., Farhoudian, A., Shushtari, Z. J., Sharhani, A., Karimi, S. E., Sayadnasiri, M., Rezaei, O., & Ghiasvand, H. (2020). Factors associated with time between using a drug and injection initiation among people who inject drugs in Kermanshah, Iran. *International Journal of Adolescent medicine and Health, 32*(5), 20170204.

Noroozi, M., Higgs, P., Bayani, A., Armoon, B., Astaneh, A. N., Moghaddam, L. F., & Askari, M. (2020). Non-fatal overdose among people who inject drugs in Tehran, Iran. *Substance Abuse Treatment, Prevention, and Policy, 15*(1), 1-7.

O'Keefe, D., Bowring, A., Aitken, C., & Dietze, P. (2018). The association between intentional overdose and same-sex sexual intercourse in a cohort of people who inject drugs in Melbourne, Australia. *Substance Use & Misuse, 53*(5), 755-762.

O'Halloran, C., Cullen, K., Njoroge, J., Jessop, L., Smith, J., Hope, V., & Ncube, F. (2017). The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs (PWID) in England, Wales and Northern Ireland. *International Journal of Drug Policy, 46*, 34-40.

Ochoa, K. C., Davidson, P. J., Evans, J. L., Hahn, J. A., Page-Shafer, K., & Moss, A. R. (2005). Heroin overdose among young injection drug users in San Francisco. *Drug and Alcohol Dependence, 80*(3), 297-302.

Otachi, J. K., Vundi, N., & Surratt, H. L. (2020). Examining factors associated with non-fatal overdose among people who inject drugs in rural Appalachia. *Substance Use & Misuse, 55*(12), 1935-1942.

Park, J. N., Weir, B. W., Allen, S. T., Chaulk, P., & Sherman, S. G. (2018). Fentanyl-contaminated drugs and non-fatal overdose among people who inject drugs in Baltimore, MD. *Harm Reduction Journal, 15*(1), 1-8.

Pizzicato, L. N., Johnson, C. C., & Viner, K. M. (2020). Correlates of experiencing and witnessing non-fatal opioid overdoses among individuals accessing harm reduction services in Philadelphia, Pennsylvania. *Substance Abuse, 41*(3), 301-306.

Powis, B., Strang, J., Griffiths, P., Taylor, C., Williamson, S., Fountain, J., & Gossop, M. (1999). Self-reported overdose among injecting drug users in London: Extent and nature of the problem. *Addiction, 94*(4), 471-478. doi: 10.1046/j.1360-0443.1999.9444712.x

Prangnell, A., Nosova, E., Milloy, M.-J., Wood, E., & Hayashi, K. (2019). The relationship between parental heavy drinking and non-fatal overdose among people who inject drugs in Vancouver, Canada. *Addictive Behaviors, 89*, 224-228.

Rafful, C., Orozco, R., Rangel, G., Davidson, P., Werb, D., Beletsky, L., & Strathdee, S. A. (2018). Increased non-fatal overdose risk associated with involuntary drug treatment in a longitudinal study with people who inject drugs. *Addiction, 113*(6), 1056-1063.

Rezaei, O., Ghiasvand, H., Higgs, P., Noroozi, A., Noroozi, M., Rezaei, F., Armoon, B., & Bayani, A. (2020). Factors associated with injecting-related risk behaviors among people who inject drugs: A systematic review and meta-analysis study. *Journal of Addictive Diseases, 38*(4), 420-437.

Riggs, K. R., Hoge, A. E., DeRussy, A. J., Montgomery, A. E., Holmes, S. K., Austin, E. L., Pollio, D. E., Kim, Y.-i., Varley, A. L., & Gelberg, L. (2020). Prevalence of and risk factors associated with nonfatal overdose among veterans who have experienced homelessness. *JAMA Network Open, 3*(3), e201190-e201190.

Roxburgh, A., Hall, W. D., Gisev, N., & Degenhardt, L. (2019). Characteristics and circumstances of heroin and pharmaceutical opioid overdose deaths: Comparison across opioids. *Drug and Alcohol Dependence, 205*, 107533. doi: 10.1016/j.drugalcdep.2019.06.035

Saini, R., Rao, R., Parmar, A., Mishra, A. K., Ambekar, A., Agrawal, A., & Dhingra, N. (2020). Rates, knowledge and risk factors of non-fatal opioid overdose among people who inject drugs in India: A community-based study. *Drug and Alcohol Review, 39*(1), 93-97.

Saleem, H. T., Likindikoki, S., Nonyane, B. A., Nkya, I. H., Zhang, L., Mbwambo, J., & Latkin, C. (2020). Correlates of non-fatal, opioid overdose among women who use opioids in Dar es Salaam, Tanzania. *Drug and Alcohol Dependence, 218*, 108419.

Schiavon, S., Hodgin, K., Sellers, A., Word, M., Galbraith, J. W., Dantzler, J., & Cropsey, K. L. (2018). Medical, psychosocial, and treatment predictors of opioid overdose among high risk opioid users. *Addictive Behaviors, 86*, 51-55.

Seal, K. H., Kral, A. H., Gee, L., Moore, L. D., Bluthenthal, R. N., Lorvick, J., & Edlin, B. R. (2001). Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. *American Journal of Public Health, 91*(11), 1842-1846.

Sergeev, B., Karpets, A., Sarang, A., & Tikhonov, M. (2003). Prevalence and circumstances of opiate overdose among injection drug users in the Russian Federation. *Journal of Urban Health, 80*(2), 212-219.

Sherman, S. G., Cheng, Y., & Kral, A. H. (2007). Prevalence and correlates of opiate overdose among young injection drug users in a large U.S. city. *Drug and Alcohol Dependence, 88*(2-3), 182-187. doi: 10.1016/j.drugalcdep.2006.10.006

Stang, A. (2010). Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *European Journal of Epidemiology, 25*(9), 603-605.

Stewart, D., Gossop, M., & Marsden, J. (2002). Reductions in non-fatal overdose after drug misuse treatment: Results from the National Treatment Outcome Research Study (NTORS). *Journal of Substance Abuse Treatment, 22*(1), 1-9.

Stoové, M. A., Dietze, P. M., & Jolley, D. (2009). Overdose deaths following previous non-fatal heroin overdose: Record linkage of ambulance attendance and death registry data. *Drug and Alcohol Review, 28*(4), 347-352. doi: 10.1111/j.1465-3362.2009.00057.x

Strathdee, S. A., West, B. S., Reed, E., Moazan, B., Azim, T., & Dolan, K. (2015). Substance use and HIV among female sex workers and female prisoners: Risk environments and implications for prevention, treatment, and policies. *Journal of Acquired Immune Deficiency Syndromes, 69*(0 1), S110.

Suffoletto, B., & Zeigler, A. (2020). Risk and protective factors for repeated overdose after opioid overdose survival. *Drug and Alcohol Dependence, 209*, 107890.

Tobin, K. E., & Latkin, C. A. (2003). The relationship between depressive symptoms and nonfatal overdose among a sample of drug users in Baltimore, Maryland. *Journal of Urban Health, 80*(2), 220-229.

Trayner, K. M., McAuley, A., Palmateer, N. E., Goldberg, D. J., Shepherd, S. J., Gunson, R. N., Tweed, E. J., Priyadarshi, S., Milosevic, C., & Hutchinson, S. J. (2020). Increased risk of HIV and other drug-related harms associated with injecting in public places: national bio-behavioural survey of people who inject drugs. *International Journal of Drug Policy, 77*, 102663.

Uusküla, A., Raag, M., Vorobjov, S., Rüütel, K., Lyubimova, A., Levina, O. S., & Heimer, R. (2015). Non-fatal overdoses and related risk factors among people who inject drugs in St. Petersburg, Russia and Kohtla-Järve, Estonia. *BMC Public Health, 15*(1), 1-9.

van Beek, I., Kimber, J., Dakin, A., & Gilmour, S. (2004). The Sydney medically supervised injecting centre: Reducing harm associated with heroin overdose. *Critical Public Health, 14*(4), 391-406.

Wallace, B., Kennedy, M. C., Kerr, T., & Pauly, B. (2019). Factors associated with nonfatal overdose during a public health emergency. *Substance Use & Misuse, 54*(1), 39-45.

Walley, A. Y., Cheng, D. M., Coleman, S. M., Krupitsky, E., Raj, A., Blokhina, E., Bridden, C., Chaisson, C. E., Lira, M. C., & Samet, J. H. (2014). Risk factors for recent nonfatal overdose among HIV-infected Russians who inject drugs. *AIDS Care, 26*(8), 1013-1018.

Warner-Smith, M., Darke, S., & Day, C. (2002). Morbidity associated with non-fatal heroin overdose. *Addiction, 97*(8), 963-967. doi: https://doi.org/10.1046/j.1360-0443.2002.00132.x

Warner-Smith, M., Darke, S., Lynskey, M., & Hall, W. (2001). Heroin overdose: causes and consequences. *Addiction, 96*(8), 1113-1125. doi: 10.1046/j.1360-0443.2001.96811135.x

Yang, Z., Wilsey, B., Bohm, M., Weyrich, M., Roy, K., Ritley, D., Jones, C., & Melnikow, J. (2015). Defining risk of prescription opioid overdose: Pharmacy shopping and overlapping prescriptions among long-term opioid users in medicaid. *Journal of Pain, 16*(5), 445-453.

Yin, L., Qin, G., Ruan, Y., Qian, H.-Z., Hao, C., Xie, L., Chen, K., Zhang, Y., Xia, Y., & Wu, J. (2007). Nonfatal overdose among heroin users in southwestern China. *American Journal of Drug and Alcohol Abuse, 33*(4), 505-516.

Yule, A. M., Carrellas, N. W., DiSalvo, M., Lyons, R. M., McKowen, J. W., Nargiso, J. E., Bergman, B. G., Kelly, J. F., & Wilens, T. E. (2019). Risk factors for overdose in young

people who received substance use disorder treatment. *American Journal on Addictions, 28*(5), 382-389.

Yule, A. M., Carrellas, N. W., Fitzgerald, M., McKowen, J. W., Nargiso, J. E., Bergman, B. G., Kelly, J. F., & Wilens, T. E. (2018). Risk factors for overdose in treatment-seeking youth with substance use disorders. *Journal of Clinical Psychiatry, 79*(3), 17m11678.

Zhou, Y., Luo, W., Cao, X., Zhang, B., & Wu, Z. (2016). Overdose of heroin and influencing factors in intravenous drug users in parts of Yunnan. *Zhonghua Liuxingbingxue Zazhi, 37*(5), 648-652.

Table and figure legends:

Table 1. Search strategy

Table 2. Risk of bias assessment using Newcastle-Ottawa scale

Table 3. Characteristics of non-fatal overdose among PWUIOs.

Table 4: Variables associated with non-fatal overdose among people who use illicit opioids

Table 5. Pooled odds ratio of variables associated with non-fatal overdose among PWUIOs.

Fig 1. PRISMA flow diagram

Figure 2. The prevalence of non-fatal overdose among PWUIOs.

Table 1: Search strategy

	PubMed
#23	((((((((((((Death, Sudden, Cardiac[MeSH Terms]) OR (Heart Arrest[MeSH Terms])) OR (non fatal overdose[Title/Abstract])) OR (Death[MeSH Terms])) OR (Fetal Death[MeSH Terms])) OR (Myocardial Infarction[MeSH Terms])) OR (difficulties with breathing[Title/Abstract])) OR (convulsions[MeSH Terms])) OR (Seizures[MeSH Terms])) OR (inability to wake up[Title/Abstract])) OR (collapsing[Title/Abstract])) OR (blue skin color[Title/Abstract])) OR (Unconsciousness[MeSH Terms])) AND (((((((Opiums Dependence[MeSH Terms]) OR (Morphine Dependence[MeSH Terms])) OR (Drug Users[MeSH Terms])) OR (Heroin[MeSH Terms])) OR (Heroin Dependence[MeSH Terms])) OR (Opioid-Related Disorders[MeSH Terms])) OR (Opiate Overdose[MeSH Terms]))
#22	((((((Opium Dependence[MeSH Terms]) OR (Morphine Dependence[MeSH Terms])) OR (Drug Users[MeSH Terms])) OR (Heroin[MeSH Terms])) OR (Heroin Dependence[MeSH Terms])) OR (Opioid-Related Disorders[MeSH Terms])) OR (Opiate Overdose[MeSH Terms])
#21	((((((((((((Death, Sudden, Cardiac[MeSH Terms]) OR (Heart Arrest[MeSH Terms])) OR (non fatal overdose[Title/Abstract])) OR (Death[MeSH Terms])) OR (Fetal Death[MeSH Terms])) OR (Myocardial Infarction[MeSH Terms])) OR (difficulties with breathing[Title/Abstract])) OR (convulsions[MeSH Terms])) OR (Seizures[MeSH Terms])) OR (inability to wake up[Title/Abstract])) OR (collapsing[Title/Abstract])) OR (blue skin color[Title/Abstract])) OR (Unconsciousness[MeSH Terms])
#20	Death, Sudden, Cardiac[MeSH Terms]
#19	Heart Arrest[MeSH Terms]
#18	non fatal overdose[Title/Abstract]
#17	Death[MeSH Terms]
#16	Fetal Death[MeSH Terms]
#15	Myocardial Infarction[MeSH Terms]
#14	difficulties with breathing[Title/Abstract]
#13	convulsions[MeSH Terms]
#12	Seizures[MeSH Terms]
#11	inability to wake up[Title/Abstract]
#10	collapsing[Title/Abstract]

#9	blue skin color[Title/Abstract]
#8	Unconsciousness[MeSH Terms]
#7	Opium Dependence[MeSH Terms]
#6	Morphine Dependence[MeSH Terms]
#5	Drug Users[MeSH Terms]
#4	Heroin[MeSH Terms]
#3	Heroin Dependence[MeSH Terms]
#2	Opioid-Related Disorders[MeSH Terms]
#1	Opiate Overdose[MeSH Terms]
	Scopus
#24	((TITLE-ABS-KEY (opiate AND overdose)) OR (TITLE-ABS-KEY (opioid-related AND disorders)) OR (TITLE-ABS-KEY (heroin AND dependence)) OR (TITLE-ABS-KEY (heroin)) OR (TITLE-ABS-KEY (drug AND users)) OR (TITLE-ABS-KEY (morphine AND dependence)) OR (TITLE-ABS-KEY (opium AND dependence))) AND ((TITLE-ABS-KEY (unconsciousness)) OR (TITLE-ABS-KEY (blue AND skin AND color)) OR (TITLE-ABS-KEY (collapsing)) OR (TITLE-ABS-KEY (inability AND to AND wake AND up)) OR (TITLE-ABS-KEY (seizures)) OR (TITLE-ABS-KEY (convulsions)) OR (TITLE-ABS-KEY (difficulties AND with AND breathing)) OR (TITLE-ABS-KEY (myocardial AND infarction)) OR (TITLE-ABS-KEY (fetal AND death)) OR (TITLE-ABS-KEY (death)) OR (TITLE-ABS-KEY (non AND fatal AND overdose)) OR (TITLE-ABS-KEY (heart AND arrest)) OR (TITLE-ABS-KEY (death, AND sudden, AND cardiac)))
#23	(TITLE-ABS-KEY (unconsciousness)) OR (TITLE-ABS-KEY (blue AND skin AND color)) OR (TITLE-ABS-KEY (collapsing)) OR (TITLE-ABS-KEY (inability AND to AND wake AND up)) OR (TITLE-ABS-KEY (seizures)) OR (TITLE-ABS-KEY (convulsions)) OR (TITLE-ABS-KEY (difficulties AND with AND breathing)) OR (TITLE-ABS-KEY (myocardial AND infarction)) OR (TITLE-ABS-KEY (fetal AND death)) OR (TITLE-ABS-KEY (death)) OR (TITLE-ABS-KEY (non AND fatal AND overdose)) OR (TITLE-ABS-KEY (heart AND arrest)) OR (TITLE-ABS-KEY (death, AND sudden, AND cardiac))
#22	(TITLE-ABS-KEY (opiate AND overdose)) OR (TITLE-ABS-KEY (opioid-related AND disorders)) OR (TITLE-ABS-KEY (heroin AND dependence)) OR (TITLE-ABS-KEY (heroin)) OR (TITLE-ABS-KEY (drug AND users)) OR (TITLE-ABS-KEY (morphine AND dependence)) OR (TITLE-ABS-KEY (opium AND dependence))
#21	TITLE-ABS-KEY (death, AND sudden, AND cardiac)
#20	TITLE-ABS-KEY (heart AND arrest)
#19	TITLE-ABS-KEY (non AND fatal AND overdose)
#18	TITLE-ABS-KEY (death)

#17	TITLE-ABS-KEY (fetal AND death)
#16	TITLE-ABS-KEY (myocardial AND infarction)
#15	TITLE-ABS-KEY (difficulties AND with AND breathing)
#14	TITLE-ABS-KEY (convulsions)
#12	TITLE-ABS-KEY (seizures)
#11	TITLE-ABS-KEY (inability AND to AND wake AND up)
#10	TITLE-ABS-KEY (collapsing)
#9	TITLE-ABS-KEY (blue AND skin AND color)
#8	TITLE-ABS-KEY (unconsciousness)
#7	TITLE-ABS-KEY (opium AND dependence)
#6	TITLE-ABS-KEY (morphine AND dependence)
#5	TITLE-ABS-KEY (drug AND users)
#4	TITLE-ABS-KEY (heroin)
#3	TITLE-ABS-KEY (heroin AND dependence)
#2	TITLE-ABS-KEY (opioid-related AND disorders)
#1	TITLE-ABS-KEY (opiate AND overdose)
	web of knowledge
#1	TI=(Opioid- Related Disorders OR Heroin Dependence OR Heroin OR Drug Users OR Morphine Dependence OR Opium Dependence OR Opiate Overdose) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years
#2	TS=(Unconsciousness OR blue skin color OR collapsing OR inability to wake up OR Seizures OR Convulsants OR difficulties with breathing OR Myocardial Infarction OR Fetal Death OR Death OR non fatal overdose OR Heart Arrest OR Death, Sudden, Cardiac) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years
#3	#2 AND #1
	Cochrane

#1	MeSH descriptor: [Opioid-Related Disorders] explode all trees
#2	MeSH descriptor: [Heroin Dependence] explode all trees
#3	MeSH descriptor: [Heroin] explode all trees
#4	MeSH descriptor: [Drug Users] explode all trees
#5	MeSH descriptor: [Morphine Dependence] explode all trees
#6	MeSH descriptor: [Opium Dependence] explode all trees
#7	MeSH descriptor: [Opiate Overdose] explode all trees
#8	MeSH descriptor: [Unconsciousness] explode all trees
#9	(blue skin color):ti (Word variations have been searched)
#10	(collapsing):ti,ab,kw (Word variations have been searched)
#11	(inability to wake up):ti,ab,kw (Word variations have been searched)
#12	MeSH descriptor: [Seizures] explode all trees
#13	MeSH descriptor: [Convulsants] explode all trees
#14	(difficulties with breathing):ti,ab,kw (Word variations have been searched)
#15	MeSH descriptor: [Myocardial Infarction] explode all trees
#16	MeSH descriptor: [Fetal Death] explode all trees
#17	MeSH descriptor: [Death] explode all trees
#18	(non fatal overdose):ti,ab,kw (Word variations have been searched)
#19	MeSH descriptor: [Heart Arrest] explode all trees
#20	MeSH descriptor: [Death, Sudden, Cardiac] explode all trees
#21	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7

#22	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23	#22 AND #23

Table 2. Risk of bias assessment using Newcastle-Ottawa scale

Study	**Selection (***●)**	**Comparability (*)**	**Exposure/outcome (*●●)**	**Method of assessment**	**Quality Assessment**
Fairbairn et al(Fairbairn et al., 2008)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Yang et al(Yang et al., 2015)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Caudarella et al(Caudarella et al., 2016)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
O'Halloran et al(O'Halloran et al., 2017)	***●	*	*●●	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Trayner, et al(Trayner et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Pizzicato et al(Pizzicato et al., 2020)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory

Fairgrieve et al(Fairgrieve et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
O'Keefe et al(O'Keefe et al., 2018)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Cheng et al(Cheng et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Fischer et al(Fischer et al., 2004)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Lowder et al(Lowder et al., 2020)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Milloy et al(Milloy et al., 2010)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Darke et al(Darke et al., 2007)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Uusküla et al(Uusküla et al., 2015)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Seal et al(Seal et al., 2001)	***			Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Bazazi et al(Bazazi et al., 2015)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Bergenstrom et al(Bergenstrom et al., 2008)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

Bonar and Bohnert(Bonar et al., 2016)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Bretteville-Jensen et al(Bretteville-Jensen et al., 2015)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Brugal et al(Brugal et al., 2002)	***•	*	*••	Newcastle-Ottawa scale adapted for cohort studies	Very Good
Brugal et al(Brugal et al., 2005)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Burke et al(Burke et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Coffin et al(Coffin et al., 2007)	***		*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Darke and Ross(Darke et al., 1997)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Darke et al(Darke et al., 2005)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Dayton et al(Dayton et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Escudero et al(Escudero et al., 2016)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Finkelstein et al(Finkelstein et al., 2016)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

Galea et al(Galea et al., 2006)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Grzebinski et al(Grzebinski et al., 2020)	***	*		Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Hakansson et al(Hakansson et al., 2008)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Hunter et al(Hunter et al., 2018)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Kilaru et al(Kilaru et al., 2020)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Kerr et al(Kerr et al., 2007)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Lagu et al(Lagu et al., 2006)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Lake et al(Lake et al., 2015)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Latkin et al(Latkin et al., 2018)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Madah-Amiri et al(Madah-Amiri et al., 2018)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Fendrich, et al(Fendrich et al., 2019)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

Martin et al(Martin et al., 2014)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
McGregor et al(Mcgregor et al., 1998)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Nam et al(Nam et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Britton et al(Britton et al., 2010)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Kinner et al(Kinner et al., 2012)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Walley et al(Walley et al., 2014)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Yule et al(Yule et al., 2018)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Yule et al(Yule et al., 2019)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Cochran et al(Cochran et al., 2017)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Ochoa et al(Ochoa et al., 2005)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Otachi et al(Otachi et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

Zhou et al(Zhou et al., 2016)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Groenewald et al(Groenewald et al., 2019)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Prangnell et al(Prangnell et al., 2019)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Rafful et al(Rafful et al., 2018)	***			Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Riggs et al(Riggs et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Blackburn et al(Blackburn et al., 2017)	***		*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Park et al(Park et al., 2018)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Noroozi et al(Noroozi et al., 2020)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Saleem et al(Saleem et al., 2020)	***	*	*	Newcastle-Ottawa scale adapted for cohort studies	Very Good
Schiavon et al(Schiavon et al., 2018)	*	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Satisfactory
Stewart et al(Stewart et al., 2002)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

Suffoletto and Zeigler(Suffoletto et al., 2020)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Tobin and Latkin(Tobin et al., 2003)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Van Beek et al(van Beek et al., 2004)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Wallace et al(Wallace et al., 2019)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good
Yin et al(Yin et al., 2007)	***	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Very Good
Sherman et al(Sherman et al., 2007)	**	*	*	Newcastle-Ottawa scale adapted for cross-sectional studies	Good

∗: For cross-section studies

•: For cohort studies

Table 3: characteristics of non-fatal overdose among PWUD

Author	participants	Sample Size	Year	Country	Study Design
Fairbairn et al(Fairbairn et al., 2008)	IDU	551	2008	Canada	Cohort
Yang et al(Yang et al., 2015)	DU	9010	2015	USA	Cross-section
Caudarella et al(Caudarella et al., 2016)	DU	2598	2016	Canada	Cross-section
O'Halloran et al(O'Halloran et al., 2017)	IDU	3850	2018	Ireland	Cross-section
Trayner, et al(Trayner et al., 2020)	IDU	1469	2020	Scotland	Cross-section
Pizzicato et al(Pizzicato et al., 2020)	DU	370	2019	USA	Cross-section
Fairgrieve et al(Fairgrieve et al., 2020)	IDU	889	2019	Canada	Cross-section
O'Keefe et al(O'Keefe et al., 2018)	IDU	757	2017	Australia	Cohort
Cheng et al(Cheng et al., 2020)	DU	599	2020	Canada	Cross-section
Fischer et al(Fischer et al., 2004)	DU	679	2004	Canada	Cross-section
Lowder et al(Lowder et al., 2020)	DU	24031	2011	USA	Cross-section
Milloy et al(Milloy et al., 2010)	**IDU**	**252**	**2010**	**Thailand**	**Cohort**
Darke et al(Darke et al., 2007)	DU	387	2007	Australia	Cohort
Uusküla et al(Uusküla et al., 2015)	IDU	588	2015	Russia and Estonia	Cross-section
Seal et al(Seal et al., 2001)	IDU	1427	2001	USA	Cross-section
Bazazi et al(Bazazi et al., 2015)	IDU	460	2015	Malysia	Cross-section
Bergenstrom et al(Bergenstrom et al., 2008)	IDU	299	2008	Vietnam	Cross-section
Bonar and Bohnert(Bonar et al., 2016)	IDU	91	2016	USA	Cross-section
Bretteville-Jensen et al(Bretteville-Jensen et al., 2015)	IDU	1355	2014	Norway	Cross-section

Brugal et al(Brugal et al., 2002)	DU	2556	2001	Spain	case-control
Brugal et al(Brugal et al., 2005)	DU	5049	2005	Spain	Cohort
Burke et al(Burke et al., 2020)	DU	2154426	2019	USA	Cohort
Coffin et al(Coffin et al., 2007)	IDU	772	2007	USA	Cross-section
Darke and Ross(Darke et al., 1997)	IDU	312	1997	Australia	Cross-section
Darke et al(Darke et al., 2005)	DU	495	2005	Australia	Cross-section
Dayton et al(Dayton et al., 2020)	IDU	372	2020	USA	Cross-section
Escudero et al(Escudero et al., 2016)	IDU	15070	2016	Canada	Cross-section
Finkelstein et al(Finkelstein et al., 2016)	DU	88553	2016	Canada	Cohort
Galea et al(Galea et al., 2006)	DU	1066	2008	USA	Cross-section
Grzebinski et al(Grzebinski et al., 2020)	DU	64426	2020	USA	Cross-section
Hakansson et al(Hakansson et al., 2008)	DU	7085	2008	Sweden	Cross-section
Hunter et al(Hunter et al., 2018)	IDU	283	2018	USA	Cross-section
Kilaru et al(Kilaru et al., 2020)	DU	6451	2020	USA	Cohort
Kerr et al(Kerr et al., 2007)	IDU	1587	2007	Canada	Cross-section
Lagu et al(Lagu et al., 2006)	DU	329	2005	USA	Cross-section
Lake et al(Lake et al., 2015)	IDU	1660	2015	Canada	Cross-section
Latkin et al(Latkin et al., 2018)	DU	450	2018	USA	Cross-section
Madah-Amiri et al(Madah-Amiri et al., 2018)	DU	1054	2018	Norway	Cross-section
Fendrich, et al(Fendrich et al., 2019)	DU	368	2019	USA	Cross-section
Martin et al(Martin et al., 2014)	DU	607	2014	Canada	Cross-section

McGregor et al(Mcgregor et al., 1998)	DU	218	1998	Australia	Cross-section
Nam et al(Nam et al., 2020)	DU	246466	2020	USA	Cohort
Britton et al(Britton et al., 2010)	DU	3900	2010	USA	Cross-section
Kinner et al(Kinner et al., 2012)	DU	2515	2012	Canada	Cohort
Walley et al(Walley et al., 2014)	IDU	294	2014	Russia	Cross-section
Yule et al(Yule et al., 2018)	DU	200	2018	USA	Cross-section
Yule et al(Yule et al., 2019)	DU	127	2019	USA	Cross-section
Cochran et al(Cochran et al., 2017)	DU	382828	2019	USA	Cross-section
Ochoa et al(Ochoa et al., 2005)	IDU	759	2005	USA	Cross-section
Otachi et al(Otachi et al., 2020)	IDU	324	2020	USA	Cross-section
Zhou et al(Zhou et al., 2016)	IDU	340	2016	china	Cross-section
Groenewald et al(Groenewald et al., 2019)	DU	1146412	2019	USA	Cohort
Prangnell et al(Prangnell et al., 2019)	IDU	327	2018	Canada	Cross-section
Rafful et al(Rafful et al., 2018)	IDU	671	2018	Mexico	Cross-section
Riggs et al(Riggs et al., 2020)	DU	5766	2020	USA	Cross-section
Blackburn et al(Blackburn et al., 2017)	IDU	1203	2017	Vietnam	Cross-section
Park et al(Park et al., 2018)	IDU	203	2018	USA	Cross-section
Noroozi et al(Noroozi et al., 2020)	IDU	465	2020	Iran	Cross-section
Saleem et al(Saleem et al., 2020)	DU	200	2021	Tanzania	Cross-section
Schiavon et al(Schiavon et al., 2018)	DU	244	2018	USA	Cross-section
Stewart et al(Stewart et al., 2002)	DU	753	2002	England	Cross-section

Suffoletto and Zeigler(Suffoletto et al., 2020)	DU	4155	2020	USA	Cohort
Tobin and Latkin(Tobin et al., 2003)	DU	729	2003	USA	Cross-section
Van Beek et al(van Beek et al., 2004)	IDU	3747	2004	Australia	Cross-section
Wallace et al(Wallace et al., 2019)	IDU	187	2018	Canada	Cross-section
Yin et al(Yin et al., 2007)	DU	731	2007	china	Cross-section
Sherman et al(Sherman et al., 2007)	IDU	39	2008	USA	Cross-section

Table 4: Variables associated with non-fatal overdose among people who use illicit opioids

Author	Prevalence	Age >30 years	Being female	Being homeless	Received money, goods or drugs in exchange for sex	Used a speedball	Witnessed an overdose	Public injecting	Poly drug use (more >2 drug use)	Non-injection methamphetamine use	Injecting frequency
Fairbairn et al(Fairbairn et al., 2008)	✓	✓			✓			✓		✓	
Yang et al(Yang et al., 2015)	✓										
Caudarella et al(Caudarella et al., 2016)	✓										
O' Halloran et al(O' Halloran et al., 2017)	✓				✓				✓		
Trayner, et al(Trayner et al., 2020)								✓			
Pizzicato et al(Pizzicato et al., 2020)				✓		✓	✓		✓		
Fairgrieve et al(Fairgrieve et al., 2020)										✓	
O'Keefe et al(O'Keefe et al., 2018)			✓								
Cheng et al(Cheng et al., 2020)		✓		✓						✓	
Fischer et al(Fischer et al., 2004)	✓			✓							
Lowder et al(Lowder et al., 2020)	✓										

Milloy et al(Milloy et al., 2010)	✓				✓			✓	✓		
Darke et al(Darke et al., 2007)	✓										
Uusküla et al(Uusküla et al., 2015)											✓
Seal et al(Seal et al., 2001)	✓				✓						✓
Bazazi et al(Bazazi et al., 2015)	✓									✓	
Bergenstrom et al(Bergenstrom et al., 2008)	✓	✓							✓		
Bonar and Bohnert(Bonar et al., 2016)	✓	✓									
Bretteville-Jensen et al(Bretteville-Jensen et al., 2015)	✓										
Brugal et al(Brugal et al., 2002)	✓										✓
Brugal et al(Brugal et al., 2005)	✓										✓
Burke et al(Burke et al., 2020)		✓		✓							
Coffin et al(Coffin et al., 2007)	✓	✓									
Darke and Ross(Darke et al., 1997)	✓										
Darke et al(Darke et al., 2005)	✓								✓		
Dayton et al(Dayton et al., 2020)											✓
Escudero et al(Escudero et al., 2016)	✓			✓							
Finkelstein et			✓								

al(Finkelstein et al., 2016)											
Galea et al(Galea et al., 2006)	✓			✓							
Grzebinski et al(Grzebinski et al., 2020)			✓								
Hakansson et al(Hakansson et al., 2008)	✓									✓	
Hunter et al(Hunter et al., 2018)								✓			
Kilaru et al(Kilaru et al., 2020)			✓								
Kerr et al(Kerr et al., 2007)	✓		✓	✓		✓		✓			
Lagu et al(Lagu et al., 2006)	✓						✓				
Lake et al(Lake et al., 2015)								✓	✓		
Latkin et al(Latkin et al., 2018)	✓					✓			✓		
Madah-Amiri et al(Madah-Amiri et al., 2018)								✓			
Fendrich, et al(Fendrich et al., 2019)	✓	✓	✓						✓		
Martin et al(Martin et al., 2014)	✓			✓							
McGregor et al(Mcgregor et al., 1998)	✓								✓		
Nam et al(Nam et al., 2020)			✓								

Britton et al(Britton et al., 2010)	✓										
Kinner et al(Kinner et al., 2012)	✓							✓		✓	
Walley et al(Walley et al., 2014)	✓										✓
Yule et al(Yule et al., 2018)	✓									✓	✓
Yule et al(Yule et al., 2019)	✓										
Cochran et al(Cochran et al., 2017)			✓								
Ochoa et al(Ochoa et al., 2005)	✓					✓	✓				
Otachi et al(Otachi et al., 2020)	✓										
Zhou et al(Zhou et al., 2016)	✓										
Groenewald et al(Groenewald et al., 2019)	✓										
Prangnell et al(Prangnell et al., 2019)	✓			✓							
Rafful et al(Rafful et al., 2018)	✓										✓
Riggs et al(Riggs et al., 2020)				✓			✓				
Blackburn et al(Blackburn et al., 2017)											✓
Park et al(Park et al., 2018)	✓		✓	✓		✓					
Noroozi et al(Noroozi et al., 2020)	✓								✓		

Saleem et al(Saleem et al., 2020)	✓										
Schiavon et al(Schiavon et al., 2018)							✓				
Stewart et al(Stewart et al., 2002)	✓										
Suffoletto and Zeigler(Suffoletto et al., 2020)	✓		✓								
Tobin and Latkin(Tobin et al., 2003)	✓										✓
Van Beek et al(van Beek et al., 2004)	✓							✓			
Wallace et al(Wallace et al., 2019)	✓							✓			
Yin et al(Yin et al., 2007)	✓										✓
Sherman et al(Sherman et al., 2007)	✓			✓							

Table 5. Pooled odds ratio of variables associated with non-fatal overdose among PWUD.

Variables	Model	Number study	ORs, 95%CI	Degrees of freedom	*p**	I^2
Age<30 years	Random	7	1.31, 95%CI(1.16-1.48)	6.00	0.01	0.97
Being female	Random	10	1.66, 95%CI(1.01-2.73)	9.00	0.01	0.99
Being homeless	Random	12	1.64, 95%CI(1.45- 1.84)	11.00	0.14	0.32
Received money, goods or drugs in exchange for sex	Random	4	1.77, 95%CI(1.46-2.15)	3.00	0.04	0.00
Used a speedball	Random	5	1.33, 95%CI(0.85-2.08)	4.00	0.92	0.00
Witnessed an overdose	Random	5	2.22, 95%CI(1.61-3.08)	4.00	0.01	0.72
Public injecting	Random	10	1.61, 95%CI(1.37-1.89)	9.00	0.01	0.64
Poly drug use (more >2 drug use)	Random	10	1.73, 95%CI(1.44-2.07)	9.00	0.01	0.69
Non-injection methamphetamine use	Random	7	2.01, 95%CI(1.66- 2.43)	6.00	0.31	0.16
Injecting frequency	Random	12	2.66, 95%CI(1.80-3.92)	11.00	0.01	0.93

*P related to heterogeneity statistic