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REVIEW

Suicidal behaviors among intravenous drug users: a meta-analysis

Bahram Armoon[a,b], Marie-Josée Fleury[a,b], Azadeh Bayani[c], Rasool Mohammadi[d], Elaheh Ahounbar[e,f], and Mark D. Griffiths[g]

[a]Douglas Hospital Research Centre, Montreal, Quebec, Canada; [b]Department of Psychiatry, McGill University, Montreal, Quebec, Canada; [c]Student Research Committee, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [d]Department of Biostatistics and Epidemiology, School of Public Health and Nutrition, Lorestan University of Medical Sciences, Khorramabad, Iran; [e]Orygen, the National Center of Excellence in Youth Mental Health, University of Melbourne, Parkville, Australia; [f]Center for Youth Mental Health, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Parkville, Australia; [g]International Gaming Research Unit, Psychology Department, Nottingham Trent University, Nottingham, UK

ABSTRACT

Background: Suicidal behaviors including ideations and attempts may ultimately lead to suicide especially among intravenous drug users (IVDUs). The present study assessed the prevalence, sociodemographic characteristics, risky behaviors, mental health conditions, and type of drug use associated with suicidal behaviors among IVDUs.

Methods: Studies in English published from January 1, 1995 to February 1, 2022 were searched on *PubMed, Scopus, Cochrane*, and *Web of Science* to identify papers on variables associated with suicidal behaviors (ideation and attempts) among IVDUs.

Results: Out of 10,795 papers, 21 studies met the eligibility criteria. Among IVDUs, the findings indicated a past-year pooled prevalence rate of 35% for suicide ideations (95% CI, 22%–48%) and 25% for suicide attempts (95% CI, 13%–36%). Generally, suicide ideations were associated with being homeless, having a previous history of physical and sexual abuse, and depression. Suicide attempts were associated with being female, having a previous history of physical and sexual abuse, having depression or other mental health disorders (e.g., anxiety, stress, and serious mental health disorders), and having cocaine, methamphetamine, sedative-hypnotic, and polysubstance use disorders.

Conclusions: Integrated treatment and assertive community treatment approaches may be promoted to prevent suicidal behaviors. Such programs can be implemented for referring individuals to receive suicide attempt-concerned interventions and motivational therapy.

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Introduction

As a substantial and preventable health concern, suicide is the tenth major reason for death globally and imposes a significant burden on individuals (Hawton et al., 2009). In total, 1.4% of all death cases are due to suicide worldwide (Bachmann, 2018). Moreover, suicide is fourth leading cause of death in 15-19-year-olds (World Health Organization, 2021). As a result, suicide is a leading reason for premature morbidities (Poorolajal et al., 2012). Suicidal behaviors, including ideations and attempts, may ultimately lead to suicide (Crosby et al., 1999). Most suicides are attributed to mental health disorders including major depressive disorder and/or substance use disorders (Schneider, 2009).

A few studies have reported intravenous drug use as a risk factor for suicidal behaviors, Intravenous drug users (IVDUs) are 14-times more likely to engage in suicidal behaviors compared to the general population, and four times more at risk of experiencing suicidal attempts compared to non-injecting drug users (Wilcox et al., 2004). A meta-analysis reported that the overall suicide mortality rate among IVDUs was 14 times greater compared to non-drug users (Harris et al., 1997). Life time prevalence of suicide ideations and suicide attempts have been estimated to be as high as 37% and 47% among IVDUs respectively (Stewart et al., 2018).

The excessive risk for suicidal behaviors among IVDUs may be due to their higher exposure to risk factors of suicide (Darke et al., 2004). Previous studies have associated increased suicidal behaviors with sociodemographic variables such as being female (Darke et al., 2004), being homeless (Havens et al., 2006), engaging on risky behaviors such as needle-sharing (Sarin et al., 2013), experiencing physical and sexual abuse (Sarin et al., 2011), using drugs like methamphetamine (Marshall, Galea, et al., 2011) or cocaine (Darke et al., 2004), and having concurrent disorders such as depression (Malbergier et al., 2001).

To the best of the present authors' knowledge there is only one previously published meta-analysis and this was restricted to the correlation between alcohol use disorders and co-occurring bipolar disorder and suicide attempts (Carrà et al., 2014). However, a significant body of literature has examined suicidal behaviors among IVDUs but has provided inconsistent and contradictory findings. There is no meta-analysis study examining suicidal behaviors including suicide ideations and attempts and their correlates with sociodemographic characteristics, risky behaviors, mental health conditions, and type of drug use among IVDUs. Therefore, the present systematic review and meta-analysis study aimed to determine the prevalence, sociodemographic characteristics,

risky behaviors, mental health conditions, and type of drug use correlated with suicide behaviors among IVDUs.

Methods

Search strategy

The present study was carried out according to the instructions in the Protocols of Systematic Reviews and Meta-Analyses (PRISMA) (Bayani et al., 2020; Bayat et al., 2020; Rezaei et al., 2020). Two of the authors (AB and BA) independently reviewed relevant studies published between January 1st 1995 to February 1st 2022 which were identified using *PubMed, Scopus, Web of Science* and *Cochrane Library* databases. All fields within records and Medical Subject Headings (MeSH terms) were used to expand the search in these four databases. The search strategy was prepared and modified for the various databases using important Boolean operators (AND/OR) with initial keywords *"(suicide ideations), (suicide attempts), (suicidal behaviors), (injecting drug use), (substance abuse, intravenous)".* Finally, references of the included papers were searched by hand for further relevant studies (**Supplementary File 1)**.

Inclusion and exclusion criteria

All studies had to meet PECOS (population, exposures, comparison, outcome, and study design) criteria. For the "population", only IVDUs was included; the "exposures" comprised positive and protective association of the sociodemographic characteristics, risky behaviors, mental health conditions, and type of drug use of IVDUs on suicidal behaviors in the past year; the "comparison" group was IVDUs without any suicidal behaviors in the past year; "outcomes" were suicide ideations or suicide attempts among IVDUs in the past year; and "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 excluded.

Screening and data extraction

Paper references were managed using *EndNote X7* software (*Thomson Reuters*). Initially, the duplicated titles/abstracts (89% agreement) were removed. First, two co-authors reviewed the paper titles and abstracts independently, based on the PECOS criteria. The agreement beyond chance (unweighted kappa) was also used for the quality evaluation process produced by BA and AB. Poor, slight, fair, moderate, substantial, or almost perfect level of agreement was represented by the values 0, 01–0.02, 0.021–0.04, 0.041–0.06, 0.061–0.08, or 0.081-1.00, respectively (Landis et al., 1977). A third member of the research team (EA) provided input as needed and helped in solving disagreements about papers included in the study. Second, [co-authors] AB and BA reviewed the full papers retained, considering the study inclusion criteria based on PECOS, and exclusion criteria such as no access to the full paper and missing key data. Data extraction and management were performed utilizing *Microsoft Excel* software. The following information was systematically documented: publication year, the study location, the author's name, the design of the study, the statistical analysis method, the study sample size, the key statistical data, and any outcome measures.

Quality appraisal of studies

The quality appraisal tool was derived from the Newcastle-Ottawa Scale (NOS) (Ghiasvand et al., 2020; Ghiasvand et al., 2019; Peterson et al., 2011). The NOS comprises three domains of (i) selection (three items for cross-sectional studies; four items for cohort studies), (ii) comparability (one item for both cross sectional studies and cohort studies), and (iii)

exposure/outcome (one item for cross-sectional studies and three items for cohort studies). The selection domain refers to the (a) representativeness of the exposed group, (b) selection of the non-exposed group, and (c) ascertainment of exposure. The comparability domain refers to the comparability of groups on the basis of the design or analysis, and the exposure/outcome domain refers to the assessment of the outcome. If a study had each item, it got a score or star. A maximum of five and eight for the quality scores of cross-sectional and cohort studies were obtained by adding the items respectively. Cross-sectional studies with a total score of 0–2, 3, 4 and 5 points were recorded as "unsatisfactory," "satisfactory," "good," or "very good" respectively." Cohort studies with a total score of 0–3, 4, 5-6 and 7-8 points were recorded as "unsatisfactory," "satisfactory," "good," or "very good" respectively" **(Supplementary File 2)**.

Data synthesis and statistical analysis

The meta-analysis was carried out by generating pooled odds ratios (ORs) and 95% confidence intervals (CIs) on identifying factors related to suicidal behaviors (ideations and attempts) among IVDUs. The OR was calculated applying a 2 × 2 table, and OR < 1 indicates a positive association between independent variables and suicidal behaviors. An OR > 1 indicates a protective association between variables. An inverse variance weighting was implemented to compute summary effect sizes. These values were indicated by regression coefficients for the multivariate analyses. Moreover, there was a variation in actual effect sizes among the studies with random effects models. Therefore, a random-effects model was employed to conduct model selection and publication bias meta-analyses. Accordingly, two uncertainty sources were considered: within-study sampling error and between-study variance. The large Cochran's Q statistics with small *p*-values and large I^2 statistics were employed to suggest the heterogeneity in true effect sizes across the papers. Publication bias was evaluated by funnel plots, trim-and-fill

analysis, and Rosenthal's fail-safe number. For data analysis, R 3.5.1 with the "meta" package was used to conduct the meta-analysis.

Results

Study characteristics

10,810 papers were found through the four database searches. After paper duplicates (4,232) were excluded, title and abstracts of 6,578 studies were screened. Of those, 128 studies were found related to the aim of study and after a full text review, 107 studies were excluded. The main reasons for exclusion were: 17 studies did not meet the quality appraisal score (16%), and 90 studies utilized a non-quantitative methodology or did not report parametric measurements such as coefficients, or odd ratios of relative risks of determinants of study outcomes (84%). Following exclusions, 21 studies remained for meta-analysis (Armstrong et al., 2014; Artenie et al., 2015; Backmund et al., 2011; Cheek et al., 2016; Chen et al., 2010; Darke et al., 2004; Darke et al., 2013; Fournier et al., 2018; Gu et al., 2014; Havens et al., 2006; Havens et al., 2004; Jin et al., 2013; Lau et al., 2018; Liu et al., 2014; Lloyd et al., 2007; Malbergier et al., 2001; Marshall, Galea, et al., 2011; Marshall et al., 2013; Sarin et al., 2011; Stewart et al., 2018; Xu et al., 2017) **(Supplementary File 3).**

Selected studies were from four WHO regions (10 from the America region [n=21,053 participants], one from the European region [n=1,409 participants], two from South-East Asia [n=763 participants] and eight from the Western Pacific region [n=2,828 participants]). The USA had the highest number of papers, with five studies (n=15,006 participants). Considering country income level, 13 studies (n=196,298) were conducted within high-income countries, six (n=10,528) within upper-middle-income countries and two (n=586) within lower middle-income countries. The sample sizes ranged from 60 to 10,203 participants. Most studies were published

between 2010 and 2017 and conducted in the USA. Two cohorts and 19 cross-sectional studies were identified. Of the 19 studies, 15 were considered of high quality **(Table 1).**

Table 1 near here

Prevalence of suicidal behaviors among intravenous drug users

Fig 1 and **Fig 2** show a significant pooled prevalence rate of 35% for suicide ideations (95% CI, 22%-48%) and 25% for suicide attempts (95% CI, 13%-36%) among IVDUs.

Figures 1 and 2 near here.

Sociodemographic characteristics, risky behaviors and mental health condition associated with suicidal behaviors among intravenous drug users

Results showed that there were no associations between suicide ideations among IVDUs and being female (OR=1.16, 95%CI=0.58-2.31). Among IVDUs who were women, 60% were more likely than men to have suicide attempts (OR=1.60, 95%CI=1.34-1.91). IVDUs who were homeless were 4.74 times more likely than who were not to report suicide ideations during the past year (OR=4.74, 95%CI=2.63-8.55).

Significant associations were found between history of physical and sexual abuse and suicidal behaviors among IVDUs. Moreover, IVDUs who had history of physical and sexual abuse were 1.95 (OR=1.95, 95%CI=1.52-2.49) and 3.53 (OR=3.53, 95%CI=2.0-6.22) times and 2.30 (OR=2.30, 95%CI=1.54-3.42) and 2.18 (OR=2.18, 95%CI=1.55-3.07) times more likely than those who did not to report suicide ideations and attempts during the past year, respectively. There was no significant association found between needle-sharing and suicide ideations among IVDUs (OR=1.39, 95%CI=0.77-2.48).

Participants with depression were 1.82 (OR=1.82, 95%CI=1.28-2.58) and 1.40 (OR=1.40, 95%CI=1.15-1.70) times more likely than those who did not to have suicide ideations and attempts in the past 12 months respectively. Also, IVDUs with mental health disorders were 2.02 (OR=2.02, 95%CI=1.48-2.75) times more likely to report suicide in the past 12 months than those who did not. There was no significant association between stigma and suicide ideations among IVDUs (OR=1.36, 95%CI=0.73-2.54) (Figures 3 and 4).

Figures 3 and 4 near hear

Type of drug use associated with suicide attempts among intravenous drug users

Significant associations were found between cocaine, methamphetamine, sedative-hypnotic and polysubstance use disorders, and suicide attempts among IVDUs. Moreover, IVDUs with cocaine, methamphetamine, sedative-hypnotic and polysubstance use disorders were 2.31 (OR=2.31, 95%CI=1.65-3.22), 1.52 (OR=1.52, 95%CI=1.06-2.18), 2.05 (OR=2.05, 95%CI=1.65-2.56), and 1.42 (OR=1.42, 95%CI=1.23-1.65) times more likely respectively to have had suicide attempts in the previous 12 months than those who did not. There was no significant association between heroin use disorder and suicide attempts among IVDUs (OR=1, 95%CI=0.74-1.34) (Figure 5).

Figure 5 near hear

Publication bias

To identify potential publication bias, the Egger's test and graph were performed. Considering the symmetry assumption, there was no significant publication bias in the reviewed studies selected for inclusion. As regards the funnel plot, the distribution of the papers was not

oriented and for most of them. In fact, it was identical, confirming no publication biases observed in the study. The publication bias test indicated considerable bias based on Egger's test (coefficient = 3.66, *p*-value < 0.001).

Discussion

The present meta-analysis explored variables associated with suicidal behaviors among intravenous drug users (IVDUs). Generally, suicide ideations were associated with being homeless, having a previous history of physical and sexual abuse, and having depression. Suicide attempts were associated with being female, having a previous history of physical and sexual abuse, having depression and mental health disorders (including anxiety, stress and serious mental health disorders), and having cocaine, methamphetamine, sedative-hypnotic, and polysubstance use disorders. The pooled prevalence of suicide ideations and attempts among study participants was 35% and 25%, respectively. These findings were higher than the percentages (35% and 20%) reported in a previous meta-analysis (Armoon et al., 2021), which reported that IVDUs might have several mental health disorders or risky behaviors which lead them to experience suicidal behaviors especially suicide attempts compared to non-injection drug users.

Regarding sociodemographic characteristics, the frequency of suicide attempts was greater among women which is consistent with the findings of international investigations, suggesting a higher risk of suicidal attempts among females with substance use disorders than their male counterparts (Backmund et al., 2011; Darke et al., 2004). Furthermore, other studies highlighted an enhanced female-wise risk of suicide attempts (OR 1.8) in the general population (Heshusius, 1980). According to the WHO, most female suicide attempts cases are related to non-suicidal motivation. Instead, they attempted suicide to convey their distress to others to modify their behaviors toward them (Hawton, 2000). In the present study, women did not report suicide

ideations, although only two studies considered being female and suicide ideations. Therefore, further studies are required to make a more definitive conclusion, because this may be due to the approaches in which females deal with their problems (Ibrahim et al., 2017). Women tend to share their experiences and feelings with others, so it may reduce their suicide ideations (Murphy, 1998). Another potential consequence of intravenous drug use – homelessness – was strongly associated with suicide ideations among IVDUs. This is in accord with previous studies of IVDUs in which homelessness was significantly associated with suicide ideations compared with non-injecting drug users (Armstrong et al., 2014; Havens et al., 2006). A systematic review and meta-analysis study (Ayano et al., 2019) comprising 27497 homeless individuals in 20 studies suggested a pooled current prevalence for suicide ideations and suicide attempts of 18% (13%-38%) and 9% (4%-33%, respectively. In addition, there was an association between a history of suicide attempts and an elevated risk of homelessness (Nilsson et al., 2019).

In relation to risky behaviors, there was a robust association between a history of physical and sexual abuse and an enhanced risk of suicidal behaviors. This finding was in line with those of some cross-sectional studies that outlined physical and sexual abuse histories as critical suicide-related risk factors (Brown et al., 1999; Twomey et al., 2000). It is recommended that histories of physical and sexual abuse are included in healthcare settings. Clinical, epidemiological, and genetic studies have specifically addressed etiologic procedures where childhood maltreatment aggravates the risk of suicidal behaviors. According to prior research data, childhood traumatic experiences and stress can present significant negative impacts on the development of the brain, leading to high vulnerability of generating psychopathological symptoms (Teicher et al., 2002).

In the present study, significant risk factors for suicidal behaviors were depression and mental health disorders. At least one type of mental health disorder, such as major depressive

disorder or bipolar disorders (Isometsä, 2014), anxiety disorders (Sareen et al., 2005), personality disorders (Bertolote et al., 2004), schizophrenia (Hor et al., 2010), and substance use disorders (Mościcki, 2001) has been diagnosed in more than 90% of completed suicide cases. In this respect, some approaches, such as intensive case management and assertive community treatment, have been demonstrated to reduce suicidal behaviors in these populations (Wang et al., 2015). According to (Dumais et al., 2005), an increased risk of suicide and recent alcohol or substance use, impulsiveness, and aggressiveness traits were associated among patients with depression. Alcohol use disorders and depression adversely impact support networks and function, resulting in elevated suicidal ideations. The first-line treatment for preventing suicidal behaviors consists of early diagnosis and providing pharmacological and non-pharmacological healthcare services to individuals with substance use disorders and depressive disorders.

In relation to type of drug use, the association between suicide attempts and cocaine and methamphetamine use were consistent with a large body of previous literature. The relevant results suggested a three-times greater risk for suicide attempts at a 12-month follow-up among individuals who primarily used cocaine (Britton et al., 2010). As found in Canada among individuals with substance use disorders, there was a significant relationship between an 80% elevated risk of suicide attempts (adjusted hazard ratio: 1.8) and methamphetamine injection (Marshall, Galea, et al., 2011). The same study reflected an association between polysubstance use and cocaine use and an increased risk of suicide attempts. These data concerned individuals with long-term cocaine abuse who presented multiple suicide risk characteristics. Furthermore, the extents of suicidal behaviors data outlined by the assessments conducted among cocaine users accepting treatment can be generalized to wide-ranging cocaine consumers. The risk of restricted social networks (leading to limited social support systems) users is higher among

methamphetamine users compared to individuals who use other types of substances (Shaw et al., 2008). Additionally, further barriers may be encountered by methamphetamine users for accessing the necessary biosocial care (Marshall, Shoveller, et al., 2011; Noroozi et al., 2020). For instance, treatment plans and support services designed for opioid injectors may be inappropriate for implementation in this group because these programs might not particularly address the healthcare needs for managing this type of substance abuse (Marshall, Galea, et al., 2011). In the present study, suicidal behaviors were common among cocaine users and polysubstance users. Among long-term drug users and polysubstance users, this is not surprising. This finding is in line with a previous meta-analysis (Armoon et al., 2021). One reason for increasing suicidal behavior risk associated with sedatives and hypnotics might be that these drugs may drive aggressive behaviors (Waern, 2003). In addition, interactions between sedatives and hypnotics and alcohol might exacerbate impulsive behaviors tendencies, which may increase the risk of suicide (Ben-Porath et al., 2002). Another explanation may be that IVDUs who use these drugs may have ready access to a suicide method which could increase risk of suicide (Gunnell et al., 2000). This finding concurs with the findings of the present study suggesting an independent association between sedative-hypnotics use and suicide attempts among IVDUs.

Limitations of the present study

A limitation of the present study concerned the self-report data provided by a significant number of the included studies, which might have biased the collected data in numerous ways (e.g., memory recall bias, social desirability bias, etc.). Also, most of the included studies implemented cross-sectional study methods, preventing the establishment of causal and temporal relationships between the underlying factors and suicidal behaviors. Moreover, studies or variables included in the studies retained that were not studied enough to be included in the meta-analysis

were also not considered as associated variables of suicidal behaviors among IVDUs (i.e., younger age, marital status, frequency of injection, alcohol or cannabis use disorders, having psychiatric treatment, being in prison, family history of suicide).

Conclusions

The present study's findings are helpful for mental healthcare staff who provide services to IVDUs concerning suicide risk evaluation and the assessment of the severity of depression and substance use. Integrated treatment and assertive community treatment approaches can prevent suicidal behaviors. Such programs can be implemented for referring individuals to receive suicidal attempt-concerned interventions and motivational therapy. Respecting the timely management of suicidal ideations, pubic or community-based psychosocial interventions, and mobile outreach teams can provide services to the vulnerable groups.

The assessment of psychiatric disorders includes depressive symptoms and substance use disorders, such as cocaine, methamphetamine, and polysubstance use. Furthermore, recent trends of depressive symptoms or substance use should be explored. The results presented crucial implications for mental health experts who provide services to IVDUs. Accordingly, preventive measures could be established based on the obtained data to minimize the frequency and risk of suicidal ideation among IVDUs. Moreover, the collected findings may facilitate further research in this regard. Additionally, the present study results are beneficial for designing prevention program plans, comprising the evaluation of substance use patterns (i.e., potentially associated with the risk of suicide) to reduce the risk of suicide.

Abbreviations

Intravenous drug users (IVDUs)

Odds ratio (OR)

Confidence intervals (CI)

Newcastle-Ottawa Scale (NOS)

Population, exposures, comparison, outcome, and study design (PECOS)

Protocols of Systematic Reviews and Meta-Analyses (PRISMA)

World Health Organization (WHO)

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Table 1. Characteristics of studies for suicidal behaviors among intravenous drug users (IVDUs).

						Sociodemographic characteristics		Risky behaviors			Mental health conditions			Type of drug use				
Authors	Participants	Sample size	Year	Study design	Country	Being female	Being homeless	History of physical abuse	History of sexual abuse	Needle sharing	Stigma	Depression	Other mental disorders	Cocaine use disorder	Methamphetamine use disorder	Sedative-hypnotic use disorder	Heroin use disorder	Polysubstance use disorders
Gu et al.	IVDUs	200	2014	Cross-sectional	China			*			*							
Marshall et al.	IVDUs	1634	2013	Cross-sectional	Canada			*	*									
Sarin et al.	IVDUs	343	2011	Cross-sectional	India			*		*								
Darke and Kaye.	IVDUs	183	2004	Cross-sectional	Australia	*								*				*
Armstrong et al.	IVDUs	420	2014	Cross-sectional	India		*	*	*	*		*						
Artenie et al	IVDUs	1240	2015	Cross-sectional	Canada								*	*	*	*		
Backmund et al.	IVDUs	1409	2011	Cross-sectional	Germany	*												
Chen et al.	IVDUs	488	2010	Cross-sectional	Taiwan							*	*				*	
Darke and Torok.	IVDUs	300	2013	Cross-sectional	Australia	*		*					*					*
Fournier et al.	IVDUs	1240	2017	Cross-sectional	Canada	*						*	*	*	*	*		
Liu et al.	IVDUs	2095	2014	Cross-sectional	USA	*						*						
Cheek et al.	IVDUs	10,203	2017	Cross-sectional	USA	*						*			*		*	
Marshall et al.	IVDUs	1873	2011	Cohort	Canada										*			
Havens et al.	IVDUs	2219	2004	Cross-sectional	USA				*				*					
Lau et al.	IVDUs	199	2017	Cross-sectional	China						*							
Xu et al.	IVDUs	652	2017	Cross-sectional	China	*						*						
Lloyd et al.	IVDUs	245	2007	Cross-sectional	USA			*	*			*						
Havens et al.	IVDUs	244	2006	Cross-sectional	USA		*					*						
Jin et al.	IVDUs	406	2013	Cross-sectional	China							*						
Malbergier and Guerra de Andrade.	IVDUs	60	2001	Cross-sectional	Brazil							*						
Stewart et al.	IVDUs	400	2018	Cohort	Australia							*	*					

*: Variables included in the final analysis

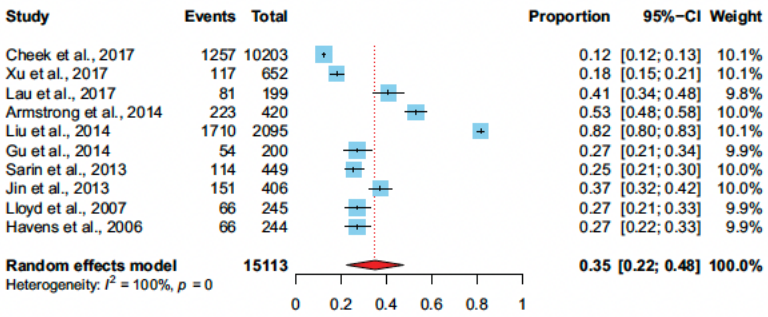

Figure 1. The prevalence of suicide ideations among intravenous drug users.

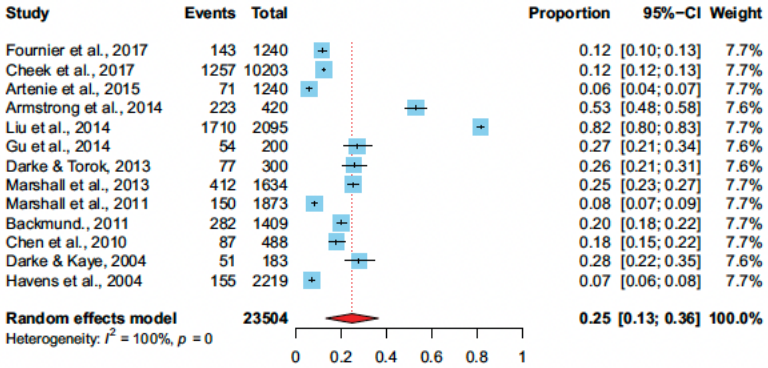

Figure 2. The prevalence of suicide attempts among intravenous drug users.

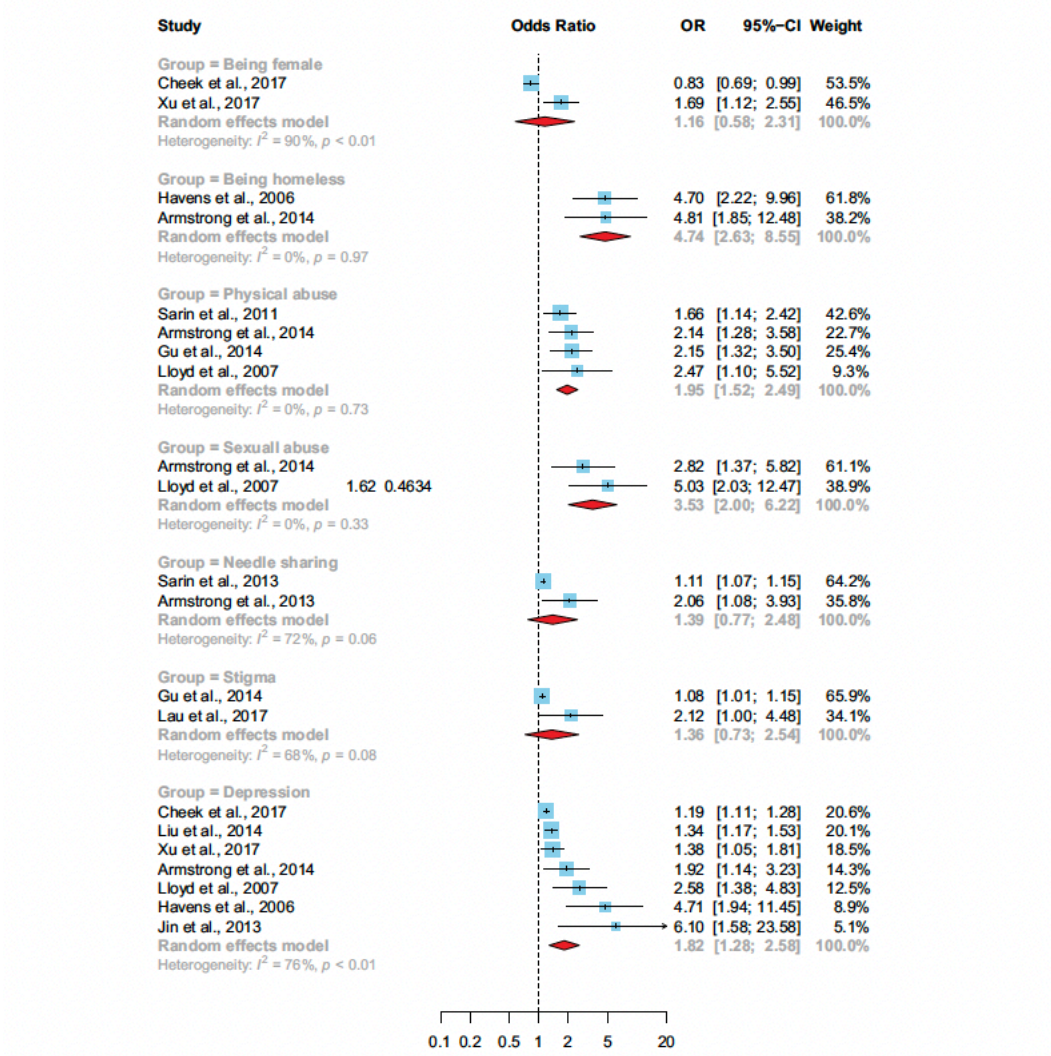

Figure 3. Pooled odds ratio of sociodemographic characteristics, risky behaviors and mental health conditions associated with suicide ideations among intravenous drug users.

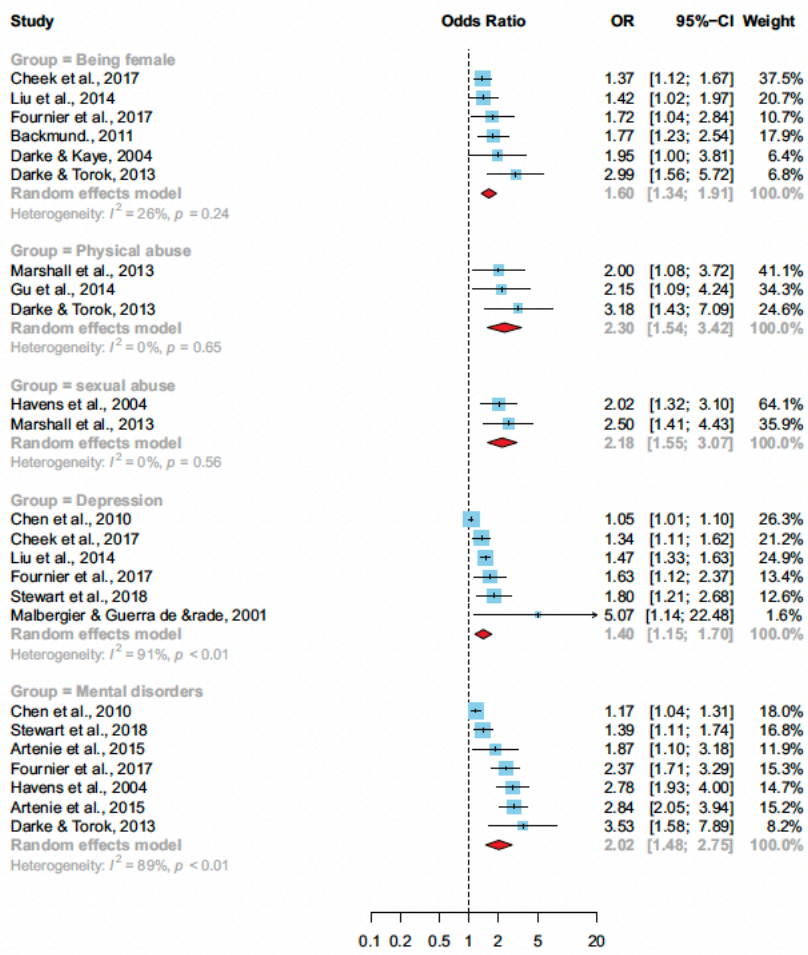

Figure 4. Pooled odds ratio of sociodemographic characteristics, risky behaviors and mental health conditions associated with suicide attempts among intravenous drug users.

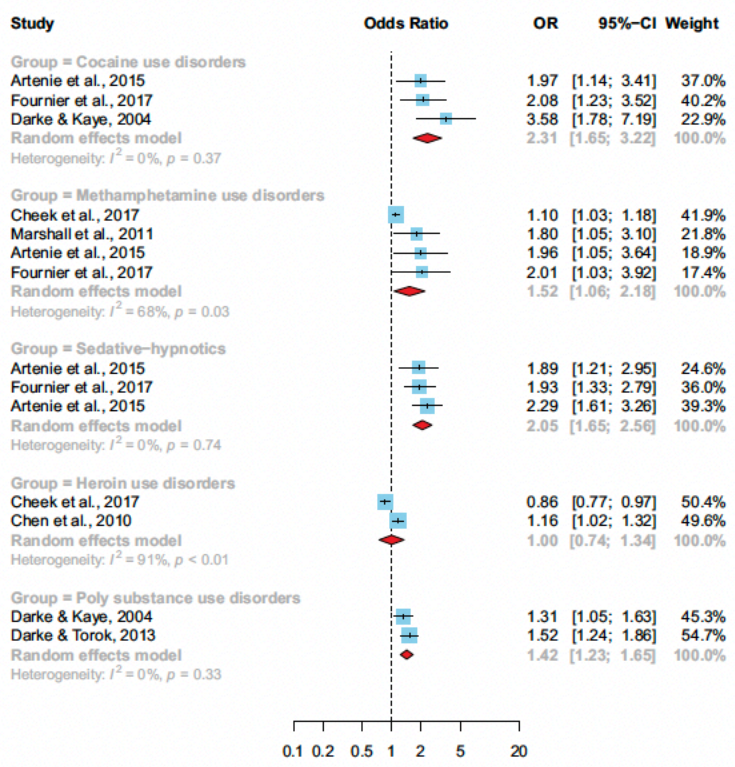

Figure 5. Pooled odds ratio of type of drug use associated with suicide attempts among intravenous drug users.