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Emergency Department Use, Hospitalization, and Their Sociodemographic Determinants among Patients with Substance-Related Disorders: A Worldwide Systematic Review and Meta-Analysis

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ABSTRACT

Background: Identifying the determinants of emergency department (ED) use and hospitalization among patients with substance-related disorders (SRD) can help inform healthcare services and case management regarding their unmet health needs and strategies to reduce their acute care. *Objectives:* The present study aimed to identify sociodemographic characteristics, type of used drug, and risky behaviors associated with ED use and hospitalization among patients with SRD. *Methods:* Studies in English published from January 1st, 1995 to April 30th, 2022 were searched from *PubMed, Scopus, Cochrane Library,* and *Web of Science* to identify primary studies on ED use and hospitalization among patients with SRD. *Results:* Of the 17,348 outputs found, a total of 39 studies met the eligibility criteria. Higher ED use and hospitalization among patients with SRD were associated with a history of homelessness (ED use: OR = 1.93, 95%CI = 1.32–2.83; hospitalization: OR = 1.53, 95%CI = 1.36–1.73) or of injection drug use (ED use: OR = 1.34, 95%CI = 1.13–1.59; hospitalization: OR = 1.42, 95%CI = 1.20–1.69). Being female (OR = 1.24, 95%CI = 1.14–1.35), using methamphetamine (OR = 1.99, 95%CI = 1.24–3.21) and tobacco (OR = 1.25, 95%CI = 1.11–1.42), having HIV (OR = 1.70, 95%CI = 1.47–1.96), a history of incarceration (OR = 1.90, 95%CI = 1.27–2.85) and injury (OR = 2.62, 95%CI = 1.08–6.35) increased ED use only, while having age over 30 years (OR = 1.40, 95%CI = 1.08–1.81) and using cocaine (OR = 1.60, 95%CI = 1.32–1.95) increased hospitalization only among patients with SRD. *Conclusions:* The finding outline the necessity of developing outreach program and primary care referral for patients with SRD. Establishing a harm reduction program, incorporating needle/syringe exchange programs, and safe injection training with the aim of declining ED use and hospitalization, is likely be another beneficial strategy for patients with SRD.

Abbreviations: CIs: confidence intervals; ED: emergency department; NOS: Newcastle-Ottawa Scale; OR: odds ratio; PECOS: Population, Exposures, Comparison, Outcome, and Study design; PRISMA: Protocols of Systematic Reviews and Meta-analyses; PWID: people who inject drugs; SRD: substance-related disorders; WHO: World Health Organization

Introduction

Patients with substance-related disorders (SRD) including patients with substance use disorders, substance intoxication, and withdrawal (American Psychiatric Association, 2013) are reported as being frequent users of emergency departments (ED) and are often hospitalized (Armoon, Grenier, et al., 2021; Fleury et al., 2022). Patients with SRD often encounter comorbid mental disorders (MD) (Kingston et al., 2017) or SRD-chronic medical conditions and suicidal

behaviors leading to increased hospitalizations and ED use (Armoon, Grenier, et al., 2021; Fleury et al., 2022). The results of a study conducted in the USA suggested that from 2014 to 2018, on average, 9.4% of all ED use and 11.9% of all hospitalizations (acute care) concerned patients with SRD (Suen et al., 2021). According to a meta-analysis study (Lewer et al., 2020), ED use and hospitalization were on average 4.8 and 7.1 times higher among patients with SRD, relative to the general population.

Hospitalization and ED use are among the most costly medical care services (Galarraga et al., 2016; Mejia de Grubb et al., 2020), which may among patients with SRD be often explained by adverse therapeutic management results (Fleury et al., 2019; Sørup et al., 2013). They could indicate limited healthcare access or poor outpatient care quality (Sørup et al., 2013). Yet, establishing alternative outpatient care plans for patients with SRD requires to know better why they use acute care, and especially their sociodemographic characteristics and risk behaviors.

To the best of the authors' knowledge, no systematic review and meta-analysis has previously explored variables associated with ED use and hospitalization among patients with SRD. A better understanding of these patient's characteristics linked with ED use and hospitalization may be beneficial for healthcare staff in improving the needs of this vulnerable population, with the aim of minimizing the use of acute care. This study results may be translated into application of adequate healthcare measures for adjusting drug policy environments. This meta-analysis study thus aimed to determine sociodemographic characteristics, type of used drugs, and risky behaviors related to ED use and hospitalization among patients with SRD.

Methods

Search strategy

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This systematic review and meta-analysis study was implemented following the instructions in Protocols of Systematic Reviews and Meta-Analyses (PRISMA) (Bayani et al., 2020; Rezaei et al., 2020). Two independent authors (BA and AB) individually reviewed relevant studies published between January 1st 1995 to April 30th 2022, identified using *PubMed, Scopus, Web of Science* and *Cochrane Library* databases. The search strategy, validated by a librarian, was prepared and modified for the various databases using important Boolean operators (AND/OR) and initial keywords *"(emergency service, hospital), (emergency department use) (hospitalization), (substance use disorders), (substance-related disorders), (drug abuse), (substance abuse, intravenous)"*. References of the included published outputs were also searched by hand for further relevant studies (**Supplementary File 1**).

Inclusion and exclusion criteria

All studies had to meet inclusion criteria based on "population, exposures, comparison, outcome, and study design" (PECOS) criteria. For "population" only patients with SRD were included; for "exposures", associated sociodemographic characteristics, type of drug used, and risky behaviors of patients with SRD on ED use and hospitalization were assessed; the "comparison" group was patients with SRD not reporting ED use and hospitalization; the "outcomes" were ED use and hospitalization among patients with SRD; and "study design" comprised cross-sectional and cohort studies (**Table 1**). The review only included studies assessing SRD with DSM or ICD diagnoses (i.e., substance use disorders, substance intoxication, substance withdrawal, and other substance-induced disorders), based on administrative databases, self-report measures or interviews. ED use or hospitalization (yes or no), the outcome measure, had related to the past six or twelve months among patients with SRD. Associated variables measured with

acute care had also to be assessed at least in two studies to be considered in the meta-analysis, this is a minimal standard considered in meta-analyses (Ryan, 2016).

Determinants and outcomes

Determinants (i.e., factors that affect outcomes) were identified in previous literature regarding patients with SRD and ED use and hospitalization. These included sociodemographic characteristics (gender, age, and history of homelessness), type of drug used (methamphetamine, tobacco, cocaine use disorder), and risky behaviors (history of injection drug use, HIV-positive status, history of incarceration and history of injury). The outcome measures were ED use and hospitalization among patients with SRD.

Table 1 near here

Data extraction procedure

Two of the authors (BA and AB) independently reviewed and evaluated the selected papers utilizing a standardized data collection checklist. The individual researchers selected the studies in a four-phase monitoring procedure. Initially, the duplicated titles/abstracts (89% agreement) meeting the Newcastle-Ottawa Scale (NOS) criteria described below were removed. Next, the papers' titles/abstracts were screened for full-text review based on the inclusion criteria of the study (96% agreement). Any disagreements between the authors were resolved by a third author (EA). Then, the full texts of selected papers were reviewed. Finally, the required data were extracted from the selected papers. Data extraction and management were performed in *Microsoft Excel* software. Data extraction included author's name, date of publication, sociodemographic characteristics (older age, being female, history of homelessness), type of drug used

(methamphetamine, cocaine, and tobacco use disorders), as well as risky behaviors (HIV-positive status, history of incarceration, and injury and history of injection).

Quality assessment of the studies

The NOS (Stang, 2010) was utilized to examine the quality of the reviewed studies (**Supplementary File 2**). This scale consisted of three domains of selection, comparability, and exposure/outcome which each included 3, 1, and 1 item for cross-sectional studies and 4, 1 and 3 for cohort studies, respectively. Publications were scored as unsatisfactory, satisfactory, good or very good. The agreement levels of poor, slight, fair, moderate, substantial, and almost perfect were considered 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 systematic review and meta-analysis was performed by generating pooled Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for determining variables associated with ED use and hospitalization among patients with SRD. The OR was computed by a 2x2 table, and an OR of <1 demonstrates a protective correlation between ED use and hospitalization and associated variables. An OR of >1 (i.e., the statistical threshold for examining correlations between outcomes and exposure variables) reflects a positive correlation between variables. To evaluate the lack of correlation between studies, the Cochran's Q test at $p<0.05$ and I square (I^2) statistics (with a cutoff point of ≥50%) were used as the most optimal choices. The 95%CI were considered for I^2. However, the negative scores were considered zero. To achieve the pooled estimation, the random-effects model was used, considering different sampling methods implemented in the studies. Additionally, sources of between-study heterogeneity were evaluated by Cochran's Q and

I[2] tests. These sources of heterogeneity were detected using subgroup analysis. Egger's and Begg's publication bias test was used in graphical and statistical dimensions to identify any existing publication bias (Begg et al., 1994; Egger et al., 1997). Baujat plots were used to identify influential effects. A *p*-value <0.05 was considered statistically significant. Subsequently, the obtained data were illustrated in forest plots. The R version 3.5.1 with the "meta" package was applied to perform the meta-analysis of the collected data (Viechtbauer, 2010).

Results

Search process and quality issues

After assessing 17,348 outputs, a total of 39 studies were included in this meta-analysis (Adam et al., 2020; Ayangbayi et al., 2017; Campbell et al., 2017; Cederbaum et al., 2014; Chen et al., 2015; Choi et al., 2016; Choi et al., 2018; Clark et al., 2013; Di Giovanni et al., 2020; Fairbairn et al., 2012; Fortney et al., 2011; Frank et al., 2015; Hope et al., 2015; Islam et al., 2013; John et al., 2017; Kerr et al., 2005; Knowlton et al., 2001; Laine et al., 2001; Larson et al., 2006; Lloyd-Smith et al., 2012; Lloyd-Smith et al., 2010; Manuel et al., 2017; Marshall et al., 2012; Mejia de Grubb et al., 2020; Olubamwo et al., 2018; Palepu et al., 2003; Palepu et al., 2005; Palepu et al., 1999; Palepu et al., 2001; Parthasarathy et al., 2005; Reddon et al., 2021; Rockett et al., 2005; Stein et al., 2003; Takahashi et al., 2007; Turner et al., 2003; Van Doren et al., 2016; Wu et al., 2012; Zhang et al., 2021; Zhu et al., 2016) **(Figure 1**). The main reasons for exclusion of studies were: 345 did not have a quantitative methodology and did not report parametric measurements such as coefficients and odd ratios of relative risks of associated variables related to the study outcomes (48%), 223 did not assess ED use or hospitalization as the study outcomes, or not as a dichotomous variable (yes or no) (32%), and 147 did not qualified according to

minimum quality appraisal (20%). As quality assessment results, 15 studies reach the "high quality" scores.

Figure 1 near here

Study characteristics

Selected studies were from three WHO regions, all conducted within high-income countries: American region (n=33, with 135,962,802 participants], European region (n=4, with 8,461 participants), and Western Pacific region (n=2, with 3,148 participant). The USA had the highest number of studies (n=23, including 135,955,462 participants) followed by Canada (n=4, including 7,335 participants). Study size at baseline had a mean of 3,488,656, with 136 as the lowest sample size (Takahashi et al., 2007), and 118,000,000 the largest number of participants (Mejia de Grubb et al., 2020), respectively. Response rates varied between studies from 65% to 100%, respectively. Patients were male at 65.45% on average in the studies, varying from 42% to 87%, and on average were 37.54 years old. Most were cohort studies (67%). The two-thirds were published between 2010 and 2021 (67%). Nine studies assessed both ED use and hospitalization as the outcomes, measured from administrative databases or self-reported questionnaire. Nineteen studies assessed ED use only, and eleven studies assessed hospitalization only as the outcome, form administrative databases, self-reported questionnaires or both administrative databases and questionnaires. Main types of drug use disorders reported in studies were polysubstance use (n=19 studies), cocaine and heroin use (n=5 studies), cannabis use (n=5 studies), cocaine use (n=2 studies), methamphetamine use (n=1 study), heroin use (n=1 study), and alcohol use disorders (n=3 studies). Three studies did not report specific type of drug use disorders, relating to SRD globally. Among the 39 studies included in the meta-analysis, 27 reported sociodemographic variables, 15 type of drug, and 19 risky behaviors (19 studies) (**Table 2**).

Table 2 near here

Results of the meta-analysis

Three significant sociodemographic variables (history of homelessness, sex and age), three type of drug use (methamphetamine, tobacco, cocaine use disorder), and four risky behaviors (history of injection drug use, HIV-positive status, history of incarceration and history of injury) were associated with ED use and/or hospitalization among patients with SRD.

Sociodemographic characteristics associated with ED use and hospitalization among patients with SRD

In eight (Ayangbayi et al., 2017; Cederbaum et al., 2014; Clark et al., 2013; Fairbairn et al., 2012; Larson et al., 2006; Palepu et al., 2003; Palepu et al., 1999; Palepu et al., 2001) and six studies out of 39 (Cederbaum et al., 2014; Olubamwo et al., 2018; Palepu et al., 2005; Palepu et al., 1999; Reddon et al., 2021; Takahashi et al., 2007), those who had a history of homelessness were reported to use ED or to be hospitalized 1.93 and 1.53 times more than non-homeless patients respectively (OR=1.93, 95%CI=1.32-2.83) (OR=1.53, 95%CI=1.36-1.73). In three studies out of 39 (Adam et al., 2020; Ayangbayi et al., 2017; Turner et al., 2003) those who were female were 1.24 times more likely than males to report ED use (OR=1.24, 95%CI=1.14-1.35). In ten studies out of 39 (Campbell et al., 2017; Cederbaum et al., 2014; Choi et al., 2016; John et al., 2017; Laine et al., 2001; Manuel et al., 2017; Mejia de Grubb et al., 2020; Olubamwo et al., 2018; Parthasarathy et al., 2005; Turner et al., 2003) patients with SRD who were older than 30 years were 1.40 times more likely than those aged 30 years or younger to be hospitalized (OR=1.40, 95%CI=1.08-1.81). There was no significant association between being older than 30 years and ED use and being

female and hospitalization among patients with SRD (OR=1.08, 95%CI=0.79-1.49) and (OR=1.11, 95%CI=0.91-1.35) (**Figures 2 and 3**).

Figures 2 and 3 near here

Type of psychoactive substances used associated with ED use and hospitalization among patients with SRD

In two studies out of 39 (Kerr et al., 2005; Marshall et al., 2012) SRD patients who used methamphetamine were 1.99 times more likely than those who did not to have ED use (OR=1.99, 95%CI=1.24-3.21). In three studies out of 39 (Campbell et al., 2017; Frank et al., 2015; John et al., 2017) patients with SRD who used tobacco were 1.25 times more likely than those who did not use tobacco to have ED use (OR=1.25, 95%CI=1.11-1.42). In six studies out of 39 (Cederbaum et al., 2014; Di Giovanni et al., 2020; Hope et al., 2015; Mejia de Grubb et al., 2020; Palepu et al., 1999; Reddon et al., 2021) those who used cocaine were 1.60 times more likely than those who did not use cocaine to be hospitalized (OR=1.60, 95%CI=1.32-1.95). There were no significant association between cocaine use and ED use among patients with SRD (OR=1.29, 95%CI=0.92-1.82). There was no significant association between methamphetamine use and hospitalization among patients with SRD (OR=0.95, 95%CI=0.76-1.19). (**Figures 4 and 5**).

Risky behaviors associated with ED use and hospitalization among patients with SRD

In three studies (Palepu et al., 2001; Stein et al., 2003; Wu et al., 2012) out of 39 (Olubamwo et al., 2018; Palepu et al., 2005; Stein et al., 2003) those who had history of injecting drugs were 1.34 and 1.42 times more likely than those without a history of injecting drugs to have ED use and to be hospitalized respectively (OR=1.34, 95%CI=1.13-1.59), (OR=1.42, 95%CI=1.20-1.69). In five studies out of 39 (Kerr et al., 2005; Knowlton et al., 2001; Lloyd-Smith

et al., 2012; Palepu et al., 1999; Palepu et al., 2001) patients who had HIV positive were 1.70 times more likely than non-HIV patients to report ED use (OR = 1.70, 95%CI = 1.47-1.96). Additionally, in two studies out of 39 (Islam et al., 2013; Manuel et al., 2017) those who reported history of incarceration were 1.90 times more likely than those who had not been incarcerated to have ED use (OR=1.90, 95%CI=1.27-2.85). Also, in three studies out of 39 (Choi et al., 2018; Larson et al., 2006; Rockett et al., 2005) those who reported history of injury were 2.62 times more likely than those who did not to have ED use (OR=2.62, 95%CI=1.08-6.35). There was no significant association between HIV-positive status and hospitalization among patients with SRD (OR=1.41, 95%CI=0.61-3.24) (**Figures 4 and 5**).

Figures 4 and 5 near here

Publication bias and influence analysis

To identify the probable publication bias, the Egger's test (Egger et al., 1997) and graph were performed. Considering the symmetry assumption, a significant publication bias among studies was noted. The publication bias test indicates considerable bias based on the Egger's test (coefficient = 3.66, p<0.001). Therefore, metatrim analysis was performed in order to remove the effect of publication bias on the pooled OR. The meta-trim analysis showed that the pooled OR was 0.21 (95%CI: 0.16–0.25) in the random effect model. Effects on the right hand side of Baujat plots showed increased heterogeneity but when the studies that had the most contribution to heterogeneity were deleted, their influence on the overall result were small (**Supplementary Files 3-10**).

Discussion

Patients with SRD with a history of homelessness or of injection drug use had higher both ED use and hospitalization. Among patients with SRD, being female, using methamphetamine or tobacco, HIV-positive status, history of incarceration or injury increased the risk of ED use only, while being older than 30 years or using cocaine the risk of hospitalization only.

The association between homelessness among patients with SRD and both high ED use and hospitalization is consistent with the literature, showing elevated risk of acute care in these populations (McGeary et al., 2000; Nambiar et al., 2018; Palepu et al., 2001). Previous findings have also identified higher odds of severe infections (Takahashi et al., 2007), acute diseases (Rickards et al., 2010), psychiatric conditions (Latimer et al., 2017), substance-induced illnesses (Magwood et al., 2020), injuries (Mackelprang et al., 2014), and suicidal behaviors (Gentil et al., 2021) among those reporting a history of homelessness, explaining high ED use and hospitalization. As people who inject drugs (PWID), prior research has demonstrated that from 69% (Fairbairn et al., 2012) to 83% (Fix et al., 2022) of them reported ED use and from 24% (Takahashi et al., 2007) to 66% (Palepu et al., 1999) hospitalization. Finally, the homeless patients may return to hospitals and ED mostly in search of shelter and meals, therefore, it is probable that they return to hospitals regardless of their health conditions (Goldberg, 2019).

Considering the association between sex and high ED use, some studies have found that from 21% (McDonald et al., 2011) to 43% (Palepu et al., 2001) of women with SRD were more likely to use ED. It might reflect more difficulty or vulnerability among women to access care (Iversen et al., 2015). It is not surprising that older age was associated with more hospitalizations, since SRD have comorbid chronic conditions, such as chronic pulmonary disease, cardiovascular disease, and metabolic dysregulation, which are higher among older patients with SRD, explaining higher hospitalization (Guaraldi et al., 2014; Oursler et al., 2011)

In relation to the types of psychoactive substances used, methamphetamine was found to be the substance with the highest odds of ED use (i.e., 1.99 times higher among patients with SRD who used methamphetamine). Previous research indicated that 11% (Nambiar et al., 2017) to 30% (Marshall et al., 2012) of patients with methamphetamine disorders used ED services. Prior studies have also highlighted the significant relationship between methamphetamine use and ED use (Hendrickson et al., 2008; Marshall et al., 2012). Methamphetamine use is associated with severe adverse outcomes, necessitating ED visits for various medical conditions (Sommers et al., 2006). The limited access to different healthcare services or the lack of appropriate treatments that comprehensively address SRD and methamphetamine use might be among other reasons for higher ED use in this group (Hendrickson et al., 2008). Studies have also found that 33% (Campbell et al., 2017) to 46% (John et al., 2017) of those who used tobacco were more likely than those who did not use tobacco to report ED use. Moreover, ED patients who use tobacco are at elevated risks of substance and problematic alcohol use, compared to different types of ED patients (McCabe et al., 2011).

In line with previous studies, there was a correlation between cocaine use and an enhanced risk for hospitalization among patients with SRD (Chang et al., 2018). Cocaine has a short half-life (40–60 min) (Degenhardt et al., 2011). Consequently, patients who use cocaine usually consume it more than 20 times on a daily basis, leading to severe systemic complications such as elevated risk of psychotic episodes, blood-borne viral infections, and cardiovascular diseases which may cause to increase hospitalization (Butler et al., 2017; Degenhardt et al., 2011; McCoy et al., 2004). Patients with cocaine use are thus prone to greater risks of intoxication and/or overdose events (Armoon, Higgs, et al., 2021; Armoon, Mohammadi, et al., 2021; Armoon et al.,

2022). Moreover, recreational cocaine use might be associated with consequences, such as aggressive behaviors and accidents, requiring acute care in patients with SRD (Fulde et al., 2015).

Regarding risky behaviors, previous studies confirmed that injection drug use is associated with increased risk of medical complications such as hepatitis C, HIV and skin and soft tissue infections which may cause to ED use and hospitalizations (Levitt et al., 2020; Ryerson et al., 2020). A large body of literature has outlined a significant association between frequent ED use and an HIV-positive status (Ng et al., 2016; Puing et al., 2020). High rates of ED use among HIV-positive patients may be due to severe conditions such as chronic obstructive pulmonary disease or comorbid infections such as soft tissue infections (Fairbairn et al., 2012; Lambert et al., 2015). Also this high rate may be explained by elevated referrals of complex profile of patients by primary care physicians to ED (Ng et al., 2016).

Another finding of the present study was that patients with SRD who experience imprisonment have a high rate of ED use. Previous research has indicated a higher rate of ED use among patients with imprisonment histories (Tuinema et al., 2019). Imprisonment might have such consequences as unplanned overdose promptly after release (Armoon, Mohammadi, et al., 2021; Binswanger et al., 2007; Møller et al., 2010) as well as restricted healthcare status follow-up, and complications with finding a job/permeant residence place (due to their criminal background) (Møller et al., 2010). Furthermore, more severe types of SRD and a more chaotic lifestyle could be associated with imprisonment. The results of the present study also indicated greater odds of ED use among patients with SRD who had a history of injury. This is consistent with the findings of previous studies (Choi et al., 2018). ED patients with cannabis and alcohol use, irrespective of age, are predisposed to abusing different harmful drugs and practice high-risk behaviors with injury consequences (Woolard et al., 2009).

Methodological considerations related to results

The studies included in the present systematic review and meta-analysis have some methodological concerns. First, one-third of the included studies were of a cross-sectional design, preventing the delineation of a causal/temporal association between the research variables under study. Second, different instruments for assessing SRD were used such as International Classification of Diseases (nine and ten revision), Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, etc. consequently, comparisons between different types of SRD are challenging. Generic instruments may be useful to be able to make comparisons between patients with SRD and the general population or other high-risk groups. Third, other variables included in the studies were also not retained in the meta-analysis as there were not presented in more than two studies (i.e., educational and marital status, hepatitis B and C infection, suicidal behaviors, stigma, unable to access services, having mental health counseling, prior hospitalization, hospital discharge). Fourth, the selected number of studies was arguably limited to the variables examined. The studies which reported sociodemographic variables associated with ED use and/or hospitalization were 10 studies (25%) for older ages, three (7%) and six studies (15%) for being women, eight (20%) and six (15%) studies for history of homelessness respectively. High heterogeneity were observed among sociodemographic variables therefore; the associations may be weak. Additionally, due to low number of studies considering sociodemographic variables, caution should be exercised when interpreting the results. Regarding psychoactive substances associated with ED use and/or hospitalization, there were six (15%) studies for cocaine use disorder each, two (5%) for methamphetamine use disorder respectively each and three studies (8%) for tobacco use disorder associated with ED use. High heterogeneity were observed among the last two mentioned variables therefore; the influence psychoactive substances needs to be very

strong to be significantly associated with acute care. Regarding risky behaviors associated with ED use and/or hospitalization, there were three (8%) and three studies (8%) for history of injection drug use, six (15%) and five studies (13%) for HIV-positive status respectively, two studies (5%) for history of incarceration and three studies (8%) for history of injury. High heterogeneity were observed among the last two mentioned variables therefore; the associations may be weak. In addition, due to low number of studies regarding risky behaviors, caution should be exercised when interpreting the results. Older age were the only variables which were considered more often, in ten studies (26%), although, these studies were not heterogeneous the reported association was strong. Other variables like employment status, duration of injection, cannabis use disorders, non-fatal overdose, and using primary care services may have influenced ED use and hospitalization, and were not addressed in studies. Finally, the heterogeneity between studies was high (in most cases). Variables (e.g., region of study, type of design, type of drug use, reasons for ED use and hospitalization, data collection source) were tested but no sources of heterogeneity were found. Participants' gender and other variables that were not evaluated may be sources of heterogeneity. Although several subgroup analyses were run to minimize the effect of heterogeneity, not all sources of heterogeneity could be taken into account in the analyses due to the fact that with more subgroup analyses, the number of studies in each subgroup decreases. Therefore, cohort or case control studies are required to establish more reliable results

Conclusions

The present study is the first systematic review and meta-analysis to study sociodemographic characteristics, type of psychoactive substances used, and risky behaviors associated with ED with use and hospitalization among patients with SRD. The key associated variables of ED use and/or hospitalization included methamphetamine and cocaine use, HIV

positives status, as well as histories of imprisonment, homelessness, and injuries. Based on the obtained data, access to outpatient health care services could be facilitated among homeless individuals with SRD by employing outreach programs. For the imprisoned patients recognizing interventions such as discharge planning, case management, and primary care referral may be effective to reduce ED use. Comprehensive care plans may be promoted for patients with SRD and a positive HIV status, targeting integrated services provided by specialized and primary healthcare staff with the target of minimizing ED use in this population. In this regard, ED liaison nurses may be advised to facilitate the referral of these patients (particularly those with cocaine and methamphetamine use) to treatment centers for substance use disorders. Establishing harm reduction programs, incorporating needle/syringe exchange programs, and safe injection training with the aim of declining ED use and hospitalization, is likely be another beneficial strategy for patients with SRD. Additionally, the study findings outlined the necessity of developing a more comprehensive strategy to be used for patients with SRD, with ED screening to address the use of other illicit drugs and providing education to this group to reduce harm. For instance, tobacco use may be a determinant for other complications associated with drug use disorders as patients are more likely to report tobacco smoking.

Abbreviations

CIs: Confidence intervals

ED: Emergency department

NOS: Newcastle-Ottawa Scale

OR: Odds ratio

PECOS: Population, exposures, comparison, outcome, and study design

PRISMA: Protocols of systematic reviews and meta-analyses

PWID: People who inject drugs

SRD: Substance-related disorders

WHO: World Health Organization

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Table 1. Inclusion and exclusion criteria.

Number	Inclusion criteria	Exclusion criteria
1-	Study had to meet PECOS criteria	Study was excluded if it comprised qualitative research
2-	Study had to be published in English (between January 1st 1995 and April 30th 2022)	Study was excluded if it was a systematic review or meta-analysis
3-	Study had to include a sample comprising patients with substance-related disorders as the main condition	Study was excluded if it had high heterogeneity or outcome variations from the considered groups
4-	Study had to include emergency department use or hospitalization as dependent variables and also sociodemographic characteristics, type of used substances, and risky behaviors as independent variables	Study was excluded if it was published as an abstract, books, thesis, or conference proceeding
5-	Study had to include multivariable analysis as analytic methods	
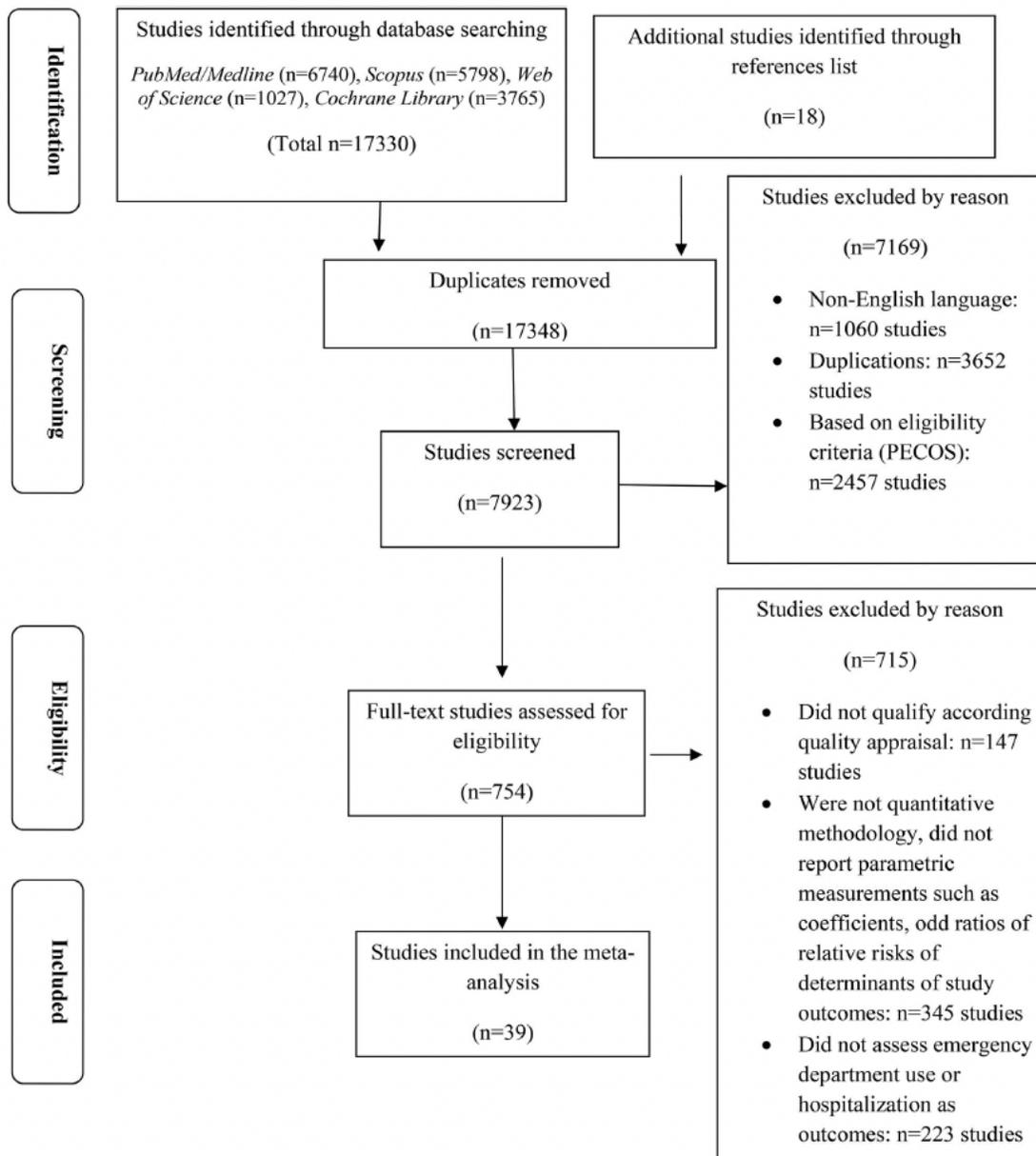
Figure 1. PRISMA flow diagram.

Table 2. Studies characteristics on emergency department (ED) use and hospitalization among patients with substance-related disorders

ED use and hospitalization studies	Author and year of publication	Years (y.) of data collections	Country	Sample at baseline	Final sample size and response rates	Study Design	Diagnostic criteria used	Type of drug use
ED use studies (n=19)	Islam et al., 2013	2013 (1 y.)	Australia	5841	2395 41%	Cross-section	NA	Polysubstance use
	Van Doren et al, 2016	2010 (1 y.)	USA	24667	24667 100%	Cross-section	ICD-9[a]	Polysubstance use
	Fairbairn et al., 2011	2005-to 08 (4 y.)	Canada	437	428 98%	Cohort	ICD-9[a]	Heroin and cocaine
	Knowlton et al., 2001	2006-08 (3 y.)	USA	287	287 100%	Cohort	NA	NA
	Kerr et al., 2004	2004-2008 (5 y.)	Canada	941	883 94%	Cohort	ICD-9[a]	Methamphetamine
	Lloyd-Smith et al., 2012	1997-2001 (5y.)	Canada	1083	1068 99%	Cohort	ICD-9[a]	Heroin and cocaine
	Marshall et al., 2012	1996 (1 y.)	Canada	427	427 100%	Cohort	NA	Polysubstance use
	Zhang et al, 2020	2016-17 (2 y.)	USA	27609	27609 100%	Cross-section	ICD-10[b]	Polysubstance use
	Wu et al, 2012	2007-09 (3 y.)	USA	113673	113673 100%	Cohort	DSM-IV[c]	Polysubstance use
	Frank et al, 2015	2008-13 (6 y.)	USA	228556	228556 100%	Cross-section	DSM-IV[c]	Polysubstance use
	Clark et al, 2013	2005-10 (6 y.)	USA	1802	1178 65%	Cohort	ICD-9[a]	Alcohol use
	Choi et al, 2017	2012-13 (2 y.)	USA	14715	14715 100%	Cross-section	ICD-9[a]	Cannabis use
	Adam et al, 2019	2006-07 and 2013 (3 y.)	Swaziland	778	630 81%	Cohort	ICD-10[b]	Alcohol use
	Ayangbayi et al, 2017	2005-2011 (7 y.)	USA	193526	193526 100%	Cross-section	CDC/NCHS[d]	Polysubstance use
	Rockett et al, 2005	1996-97 (2 y.)	USA	1890	1502 79%	Cross-section	DSM-IV[c]	Polysubstance use
	Larson et al, 2009	1997-99 (3 y.)	USA	642	470 73%	Cross-section	SAMHSA[e]	Polysubstance use
	Fortney et al, 2011	2002-04 (3 y.)	USA	217	170 78%	Cohort	DRINC[f]	Cocaine use
	Manuel and Lee, 2017	2004-11 (8 y.)	USA	14245776	14245776 100%	Cohort	ICD-10[b]	Polysubstance use
	Zhu et al, 2016	2004-11 (8 y.)	USA	2823321	2823321 100%	Cohort	DAWN/ DRV[g]	Cannabis use
Hospitalization studies (n=11)	Lloyd-Smith et al., 2010	2004-08 (5 y.)	Canada	1083	901 83%	Cohort	ICD-10[b]	NA
	Chen et al, 2015	2007-08 (2 y.)	Taiwan	789	789 100%	Cohort	DIGS-C[h]	Heroin use
	Laine et al, 2001	1996-97 (2 y.)	USA	58248	58248 100%	Cohort	ICD-9[a]	Polysubstance use
	Palepu et al, 2005	1999-2001 (3 y.)	Canada	341	341 100%	Cohort	NA	Alcohol use
	Mejia de Grubb et al, 2020	2010-14 (5 y.)	USA	118000000	118000000 100%	Cohort	ICD-9[a]	Polysubstance use
	Choi et al, 2016	2012 (1 y.)	USA	115656	115656 100%	Cross-section	ICD-9[a]	Polysubstance use
	Reddon et al, 2021	2005-15 (11 y.)	Canada	1216	1216 100%	Cohort	ICD-9[a]	Cannabis use
	Di Giovanni et al, 2020	2006-15 (10 y.)	Italy	2159	2159 100%	Cross-section	ICD-10[b]	Polysubstance use
	Hope et al., 2015	2001-2002 (2 y.)	UK	855	855 100%	Cross-section	NA	Polysubstance use
	Olubamwo et al, 2018	1997-2013 (16 y.)	Finland	4817	4817 100%	Cohort	ICD-10[b]	Polysubstance use
	Takahashi et al., 2006	2001-02 (1 y.)	USA	147	136 92%	Cohort	NA	NA
ED use and hospitalization (n=9)	Cederbaum et al, 2014	2006-09 (4 y.)	USA	73251	73251 100%	Cross-section	Addiction Severity Index and Drug Abuse Reporting Program	Polysubstance use
	Stein & Anderson, 2003	2001-2002 (2 y.)	USA	472	472 100%	Cohort	SCID[i]	Heroin and cocaine
	Palepu et al., 1999	1997-1998 (2 y.)	Canada	1103	1103 100%	Cohort	Alcohol Dependence Scale	Heroin and cocaine
	Palepu et al., 2001	2001 (1 y.)	Canada	598	598 100%	Cohort	Alcohol Dependence Scale	Cocaine
	Palepu et al., 2003	2011 (1 y.)	Canada	444	350 79%	Cohort	Alcohol Dependence Scale	Heroin and cocaine
	John and Wu, 2017	2005-13 (9 y.)	USA	16757	16757 100%	Cross-section	DSM-IV[c]	Cannabis use
	Campbell et al, 2017	2010-14 (5 y.)	USA	2752	2757 100%	Cohort	ICD-9[a]	Cannabis use
	Turner et al, 2003	1996-97 (2 y.)	USA	11556	11556 100%	Cohort	ICD-9[a]	Polysubstance use
	Parthasarathy and Weisner et al, 2005	1994-96 (3 y.)	USA	1204	1204 100%	Cohort	DSM-IV[c]	Polysubstance use

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Table 2. Continued

Reason for ED use and hospitalization	Data collection source	Percentage of ED use / hospitalization		Sociodemographic determinants			Type of drug			Risky behaviors			
				Age >30 years	Being female	History of homelessness	Cocaine use	Metham phetamine use	Tobacco use	History of injection drug use	HIV positive status	Incarceration	Injury
Any reason	Questionnaire	78%										*	
Any reason	Administrative database	NA	–	*									
Any reason	Administrative database	64%	–			*							
HIV.AIDS infection	Administrative database	33%	–								*		
Any reason	Administrative database	60%	–					*			*		
Soft tissue infection	Administrative database	27%	–								*		
Any reason	Administrative database	38%	–	*				*					
Any reason	Administrative database	NA	–	*									
Any reason	Computer-assisted self-interviewing	NA	–	*						*			
Any reason	Computer-assisted personal interviewing	NA	–	*					*				
Any reason	Administrative database	38%				*							
Any reason	Administrative database	NA	–	*									*
Any reason	Administrative database	60%	–		*								
Any reason	Administrative database	NA	–	*	*	*							
Any reason	In-person interviews	NA	–										*
Any reason	Questionnaire	47%	–			*	*						
Cocaine use	Questionnaire	NA	–				*						
Substance use	Administrative database	NA	–	*								*	
Any reason	Administrative database	NA	–	*									
Soft tissue infection	Administrative database	–	9								*		
Heroin use	Questionnaire	–	NA								*		
Illicit drug	Administrative database	–	NA	*	*								
HIV infection	Questionnaire	–	NA			*				*	*		
Any reason	Administrative database	–	NA	*	*		*	*					
HIV infection	Administrative database	–	NA	*									
Cannabis use	Administrative database	–	NA			*	*						
Any reason	Administrative database	–	NA				*						
Soft tissue infections or injuries	Computer-assisted interview	–	9.5				*						
Pneumonia	Administrative database	–	31.9	*		*				*			
Soft tissue infection	In-person interviews + Administrative database	–	40			*							
Any reason	Administrative database	NA	NA	*		*	*	*					
Any reason	Questionnaire	–	13.4				*			*			
Any reason	Questionnaire	45%	21%		*	*	*				*		
Any reason	Questionnaire	60.2%	56.2%		*	*	*			*	*		
Any reason	Questionnaire	45%	21%			*							
Any reason	Administrative database	40.15%	10.04%	*					*				
Any reason	Administrative database	87%	76%	*					*				
HIV infection	Administrative database	NA	NA	*	*								
Drug use reason	Administrative database	NA	NA	*	*								

a: International Classification of Diseases, Ninth Revision.
b: International Classification of Diseases, Tenth Revision.
c: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.
d: Centers for Disease Control and Prevention/The National Center for Health Statistics.
e: Substance Abuse and Mental Health Services Administration's cooperative agreement study on managed care for vulnerable populations.
f: The Drinker Inventory of Consequences.
g: The Drug Abuse Warning Network/ Drug Reference Vocabulary.
h: Diagnostic Interview for Genetic Studies.
i: The Structured Clinical Interview for DSM-III-R (SCID).
*variables that are included in the meta-analysis.
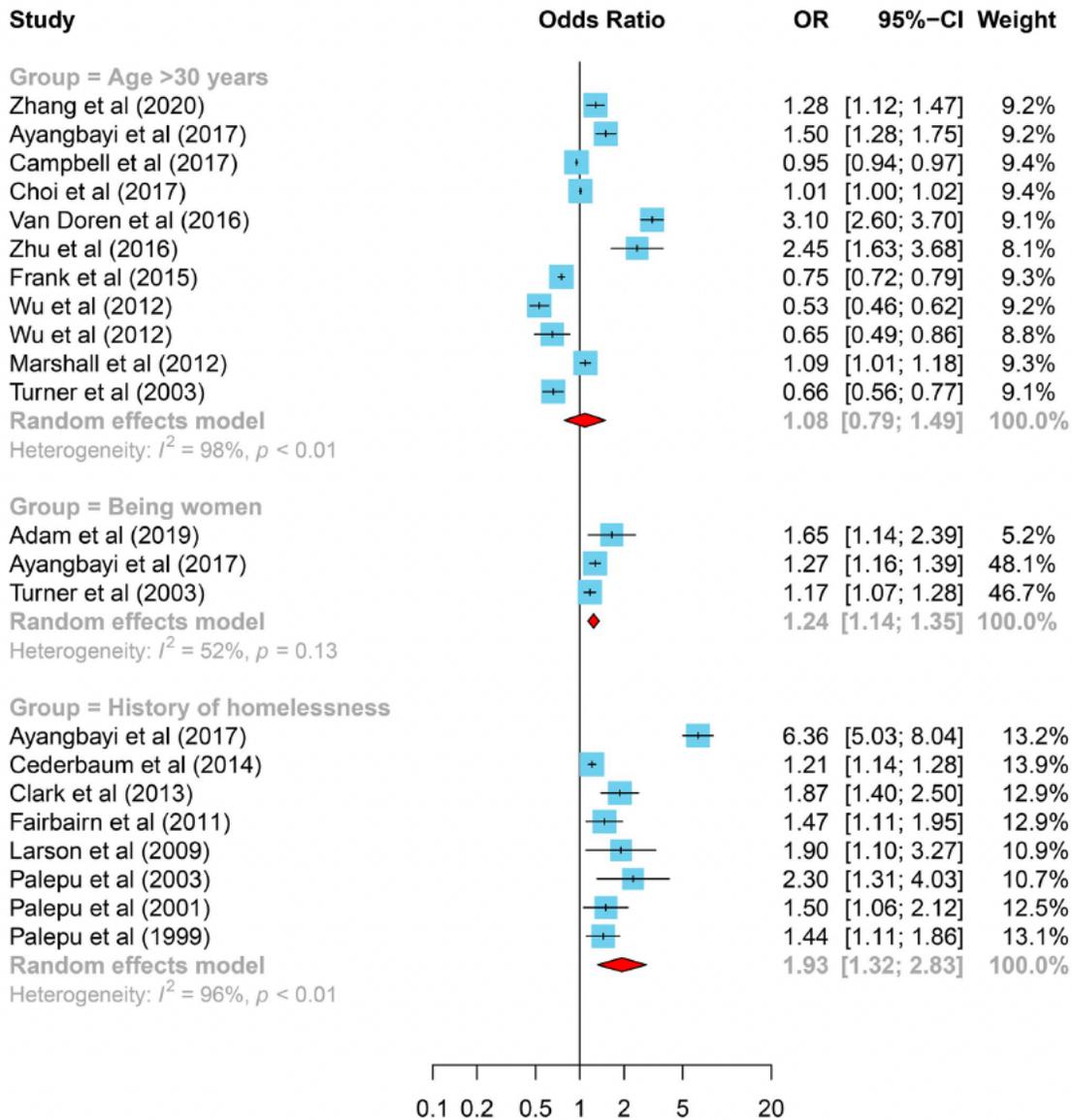
Figure 2. Pooled odds ratio of sociodemographic determinants associated with emergency department use among patients with substance-related disorders.
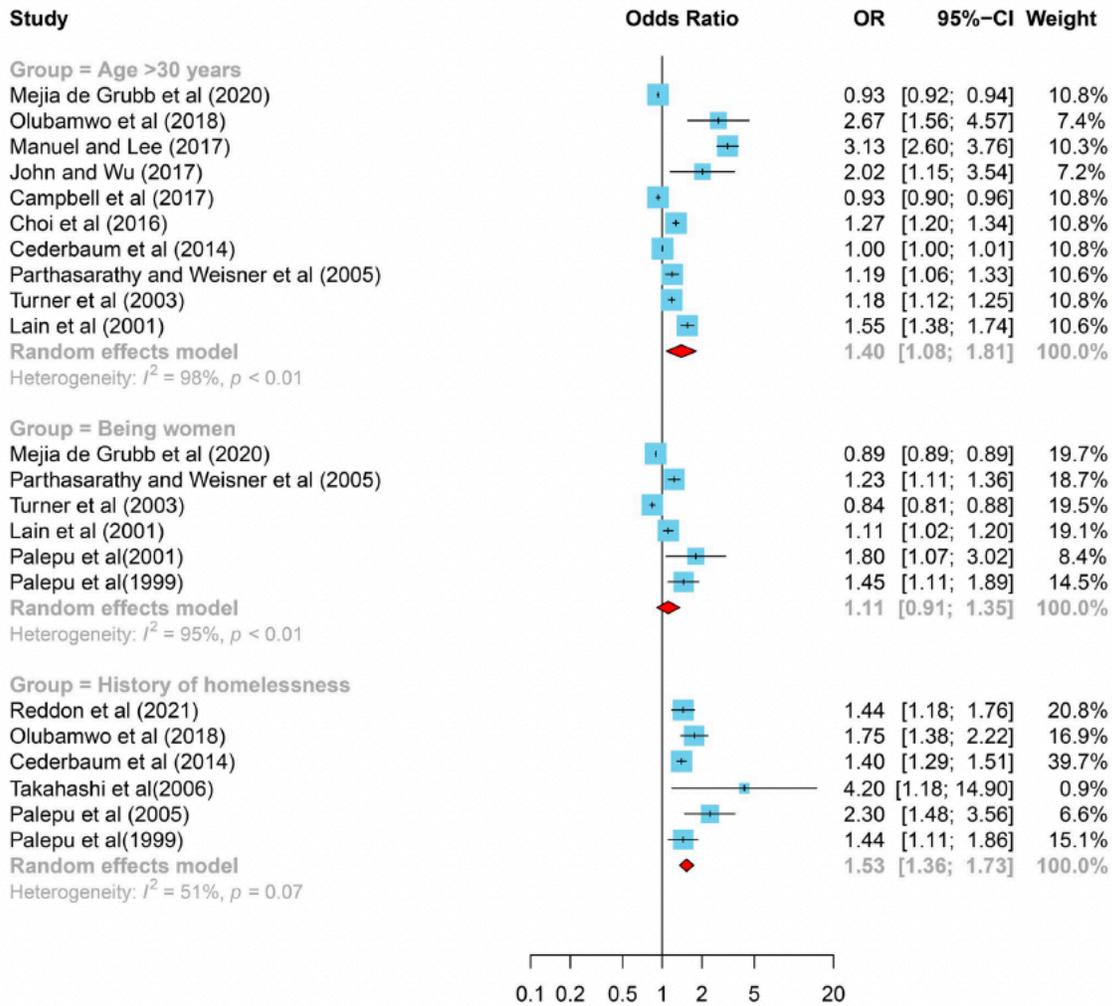
Figure 3. Pooled odds ratio of sociodemographic determinants associated with hospitalization among patients with substance-related disorders.
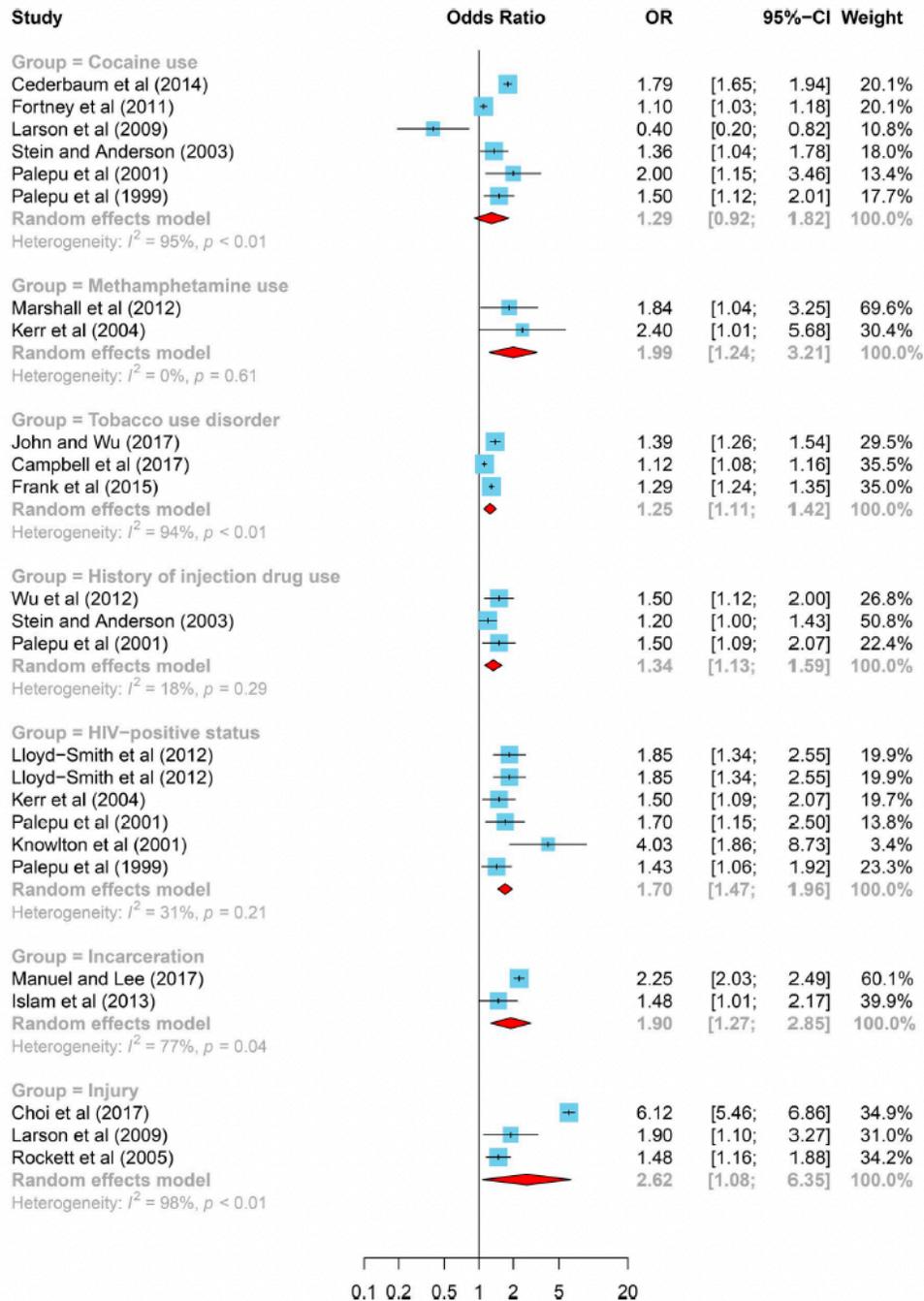
Figure 4. Pooled odds ratio of type of drug and risky behaviors associated with emergency department use among patients with substance-related disorders.
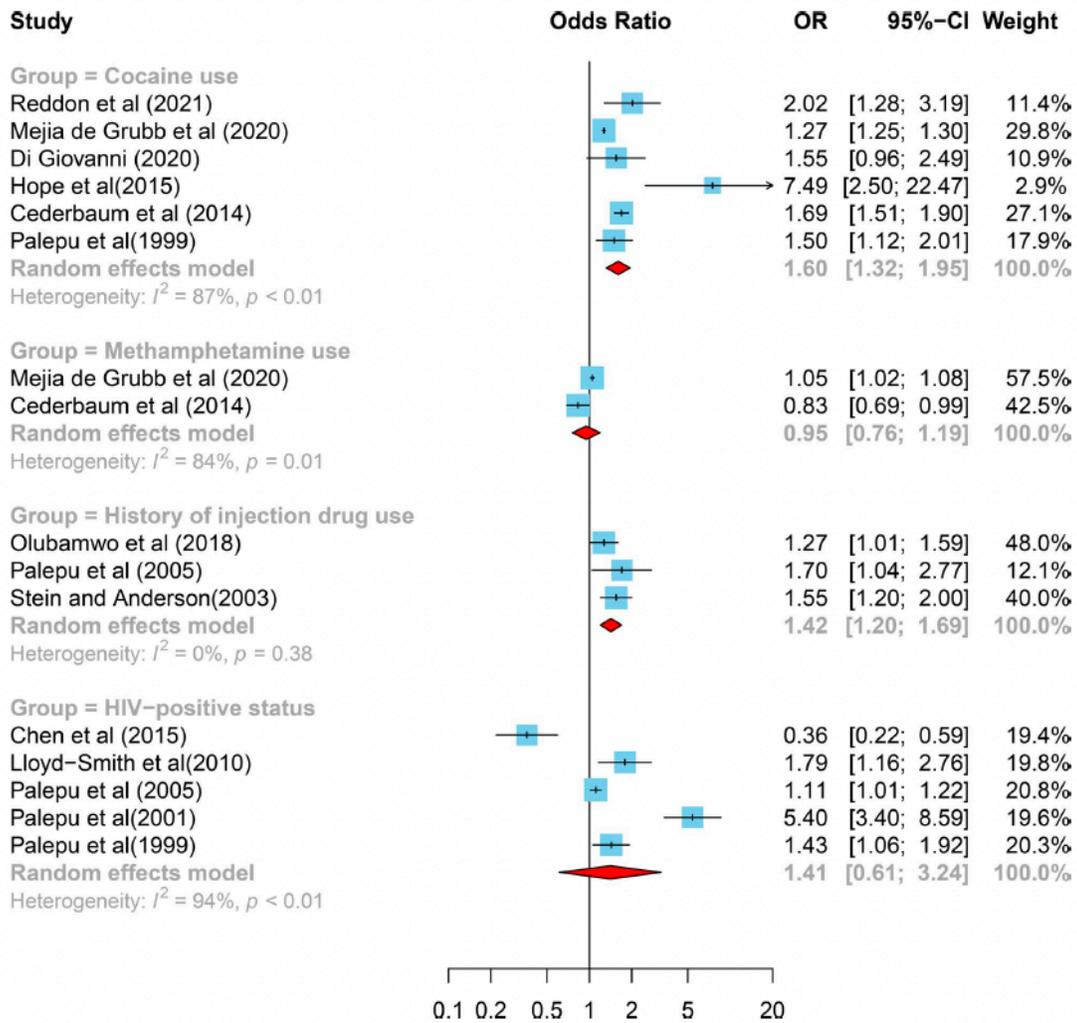
Figure 5. Pooled odds ratio of type of drug and risky behaviors associated with hospitalization among patients with substance-related disorders.