

Acute care utilization and its associated determinants among patients with substance-related disorders: A worldwide systematic review and meta-analysis

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Abstract

Introduction: Identifying determinants of emergency department (ED) use and hospitalization among patients with substance-related disorders (SRDs) can improve health services to address unmet health needs.

Aim: The present study aimed to identify the prevalence rates of ED use and hospitalization, and their associated determinants among patients with SRDs.

Methods: Studies in English published from January 1, 1995, to December 1, 2022, were searched on *PubMed*, *Scopus*, *Cochrane Library*, and *Web of Science* to identify primary studies.

Results: The pooled prevalence rates of ED use and hospitalization among patients with SRDs were 36% and 41%, respectively. Patients with SRDs who were the most at risk of being both ED users and hospitalized were those (i) having medical insurance, (ii) having other drug and alcohol use disorders, (iii) having mental health disorders, and (iv) having chronic physical illnesses. A lower level of education increased the risk of ED use only.

Discussion: To decrease ED use and hospitalization, more comprehensive services may be offered to these vulnerable patients with diversified needs.

Implications for Practice: Chronic care integrating outreach interventions could be more provided for patients with SRDs after discharge from acute care units or hospitals.

KEYWORDS

emergency department, hospitalization, substance-related disorders, mental health disorders

Introduction

Among patients with substance-related disorders (SRDs), mental health disorders (MHDs) and chronic physical illnesses are highly prevalent which often lead them to emergency department (ED) use and hospitalization (Rhee et al., 2019; Zhang et al., 2021). The 2017 National Survey on Drug Use and Health in the USA reported that approximately 74% of the adult

SRD population reported alcohol use disorders (Substance Abuse and Mental Health Services Administration, 2018). A study conducted in the USA from 2014 to 2018 suggested that patients with SRDs accounted for 9.4% of all ED use and 11.9% of hospitalizations (acute care) (Suen et al., 2022). A systematic review and meta-analysis study concluded that adults who used illicit drugs had 4.4 and 7.1 times higher rates of ED use and hospitalization, respectively, compared to the general population (Lewer et al., 2020). Another study conducted in Switzerland (Vu et al., 2015) reported that 35% of patients using ED services had SRDs in 2009-2010.

ED use and hospitalization (Galarraaga et al., 2016; Mejia de Grubb et al., 2020) are very costly, imposing a significant economic burden to societies, and are established measures of adverse outcomes if their use may be evitable (Fleury et al., 2019; Sørup et al., 2013). Moreover, ED use and hospitalization can indicate limited access to healthcare services or poor outpatient care quality (Sørup et al., 2013). Consequently, it is essential to explore sociodemographic and clinical determinants that may impact acute care use. Such knowledge could be beneficial for designing more comprehensive services to response to patient needs with SRDs.

To the best of the authors' knowledge, no previous meta-analysis has been published examining prevalence rates of ED use and hospitalization and identifying sociodemographic and clinical characteristics including types of drugs associated with acute care use among patients with SRDs. Addressing such a gap in the literature may lead to improve patient care by providing adequate information to fulfill this population's needs for preventing frequent ED use and hospitalization. This study thus aimed to determine the prevalence of ED use and hospitalization, sociodemographic and clinical determinants including types of drugs associated with ED use and hospitalization among patients with SRDs.

Methods

Search strategy

The present systematic review and meta-analysis study was implemented following the Protocols of Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). In the study selection step, two independent researchers individually reviewed the papers published between January 1, 1995 to December 1, 2022 from *PubMed*, *Scopus*, *Web of Science*, and *Cochrane Library* databases. The following search strategy keywords were validated by a librarian and adopted to each database using Boolean operators (AND/OR) and initial keywords “(*acute care*), (*inpatients*), (*health services administration*), (*emergency medical services*), (*emergency service*), (*hospital*), (*substance use disorders*), (*substance-related disorders*), (*substance abuse*, *intravenous*)”. The reference lists of the considered papers were reviewed manually as well to include more relevant papers (**Supplementary File 1**).

Eligibility criteria and study selection

The papers were managed using *EndNote X9* software. The two researchers independently reviewed the titles and abstracts based on PECOS (population, exposures, comparison, outcome, and study design) criteria. With regards to ‘population’, only patients with SRDs were included; for ‘exposures’, positive and negative associations between sociodemographic and clinical determinants including type of drug and ED use and hospitalization among patients with SRDs were assessed; the ‘comparison’ group was patients with SRD not reporting ED use and hospitalization; the ‘outcomes’ were ED use or hospitalization (‘yes’ or ‘no’ in the past 12 months) among patients with SRDs; finally, ‘study design’ integrated cross-sectional, cohort or case-control studies. The first author provided input as needed and resolved disagreement about included papers. Papers were analyzed fully, considering the study inclusion criteria based on PECO. Qualitative studies, secondary studies not written in English, studies which did not include

primary data, systematic reviews, and meta-analysis studies were excluded. Quantitative papers with high heterogeneity compared to other studies prior to the analysis (e.g., studies reporting very high/low odds ratio with a wide/narrow confidence interval compared to other studies) or outcome variations from the considered groups were also excluded (e.g., frequent use of acute care services which was not a binary assessment or where hospitalization was not the same as acute care services).

Data extraction procedure

Two researchers independently reviewed and evaluated the selected papers following a standardized data collection checklist. Data extraction and management were performed utilizing *Microsoft Excel* software. The individual researchers selected the studies in a two-phase monitoring procedure. Initially, the duplicated titles/abstracts (89% agreement) meeting the Newcastle-Ottawa Scale (NOS) criteria mentioned below were removed. Next, the papers' titles/abstracts were screened for full-text review based on the inclusion criteria of the study (96% agreement). The required data were extracted from the selected papers. The following information was systematically documented: the first author's surname, the date of publication, socio-demographics (e.g., gender, ethnicity, education levels, having medical insurance) and clinical determinants (e.g., chronic physical illnesses and having MHDs) including type of drug (e.g., alcohol, other drug, heroin and opioid use disorder). Determinants that were not analyzed in at least two studies were not included because a minimum of two studies is needed as being sufficient to be considered in a meta-analysis (Ryan, 2016).

Quality assessment of the studies

The NOS (Stang, 2010) was implemented to examine the quality of the reviewed studies (**Supplementary File 2**) in terms of exposure, outcome, and comparability with a scale comprising very good, good, satisfactory, and unsatisfactory quality domains. The NOS consists of 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 agreement levels were rated as poor (0), slight (01–0.02), fair (0.021–0.04), moderate (0.041–0.06), substantial (0.061–0.08), and almost perfect (0.081–1.00) (Landis et al., 1977). Ten studies had a high quality structure approach (Adam et al., 2020; Binswanger et al., 2008; Campbell et al., 2017; Choi et al., 2018; Hansagi et al., 2012; Larson et al., 2006; Mejia de Grubb et al., 2020; Stein et al., 2003; Turner et al., 2003; Zhang et al., 2021)

Data synthesis and statistical analysis

The present systematic review and meta-analysis research was performed by generating pooled odds ratios (ORs) and the 95% confidence intervals (CIs) for determining variables associated with ED use and hospitalization among patients with SRDs. The OR was computed using a 2x2 table, and an OR of <1 demonstrated a positive correlation between ED use and hospitalization and the target characteristic. An OR of >1 (i.e., the statistical threshold for examining the correlation between the outcome and expositive variables) reflects a strong relationship between variables and vice versa. To evaluate the lack of correlation between studies, the Q test at $p < 0.05$ and I^2 statistics (with a cutoff point of $\geq 50\%$) were the most optimal choices. A 95%CI was 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. To assess the sources of heterogeneity, subgroup analyses were run

based on year of publication of studies, country, participants' sample size, type of drugs, diagnostic criteria for SRDs and main reasons for ED use and hospitalization. Data from at least two studies were needed to explain the variable under consideration within each stratum. Sensitivity analysis was conducted using Baujat plots with a random effect model. Influential effects were detected by excluding each study from the analysis to determine their effect on the overall estimates. Egger's and Begg publication bias tests were used in graphical and statistical dimensions to identify any existing publication bias (Begg et al., 1994; Egger et al., 1997). 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 utilized to perform the meta-analysis of the collected data (Viechtbauer, 2010).

Results

Study characteristics

After a detailed assessment of over 14,348 papers, a total of 32 studies were included in the present study (Adam et al., 2020; Ayangbayi et al., 2017; Binswanger et al., 2008; 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; Frank et al., 2015; Hansagi et al., 2012; Indig et al., 2010; John et al., 2017; Knowlton et al., 2005; Laine et al., 2001; Larson et al., 2006; Manuel et al., 2017; McDonald et al., 2011; Mejia de Grubb et al., 2020; Palepu et al., 1999; Parthasarathy et al., 2005; Perron et al., 2011; Reddon et al., 2021; Rockett et al., 2005; Siegal et al., 2006; Stein et al., 2003; Turner et al., 2003; Van Doren et al., 2016; Walley et al., 2012; Wu et al., 2012; Zhang et al., 2021). The main exclusion criteria were studies that did not assess ED use or hospitalization and those that did not assess associated variables. The study selection process is illustrated in **Figure 1**.

Figure 1 here

Selected studies were from three WHO regions: America (n=26, with 133,177,907 participants], Europe (n=4, with 45,138 participants), and the Western Pacific Region (n=2, with 246,764 participants). The USA had the highest number of studies (n=24, including 133,175,588 participants). All studies were conducted within high-income countries. The lowest baseline sample size was 211 participants (Binswanger et al., 2008) and the largest was 118,000,000 (Mejia de Grubb et al., 2020) participants. The lowest response rate was 38% and the highest was 100%. Most studies (69%) were published between 2010 to 2021. Half of the studies had cohort designs and half of them had cross-sectional designs. On average, patients were more likely to be male in the studies (62.96%), varying from 44% to 87%, and were 38.8 years old. Seven studies assessed both ED use and hospitalization using administrative data (Campbell et al., 2017; Cederbaum et al., 2014; Palepu et al., 1999; Parthasarathy et al., 2005; Turner et al., 2003) or self-report survey (Rockett et al., 2005). Sixteen studies assessed ED use and nine studies assessed hospitalization only using administrative data, self-report survey or both. One-quarter of the studies reported drug use (25%) as main reason for ED use and hospitalization. Fourteen studies (44%) used the International Classification of Diseases diagnostic criteria for assessing SRDs. According to type of drug use, 22 studies polysubstance use, four cannabis use, two studies examined cocaine and heroin use, two others alcohol use, and one study cocaine use, and another one heroin use disorders. Among the 32 studies that were included in the final meta-analysis, the following variables were reported: sociodemographic variables in 17 studies, clinical variables in 21 studies, including type of drug in 11 studies (**Table 1**).

Table 1 here

Pooled prevalence rate of ED use and hospitalization among patients with SRDs

The pooled prevalence rate of ED use and hospitalization among patients with SRDs were 36% (95% CI, 26%-46%) (**Figure 2**) and 41% (95% CI, 21%-61%) (**Figure 3**) respectively.

Figures 2 and 3 here

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

In seven studies out of the 32 (Ayangbayi et al., 2017; Choi et al., 2018; Frank et al., 2015; Knowlton et al., 2005; Larson et al., 2006; Rockett et al., 2005; Zhang et al., 2021) and two studies out of 32 (Mejia de Grubb et al., 2020; Rockett et al., 2005), those who had medical insurance were 1.36 and 1.63 times more likely to report ED use or hospitalization compared to those with no medical insurance respectively (OR=1.36, 95%CI=1.05-1.74) (OR=1.63, 95%CI=1.61-1.65). In three studies out of 32 (Cederbaum et al., 2014; Chen et al., 2015; Wu et al., 2012), patients with SRDs who had a lower level of education were 1.23 times more likely to report ED use compared to those who had a high level of education (OR=1.23, 95%CI=1.03-1.48) (**Figures 4, 5**).

Figures 4 and 5 here

Type of drug associated with ED use and hospitalization among patients with SRDs

In four studies out of 32 (Cederbaum et al., 2014; Frank et al., 2015; John et al., 2017; Manuel et al., 2017) and four studies out of 32 (Cederbaum et al., 2014; Chen et al., 2015; Choi et al., 2016; John et al., 2017) patients with SRDs who had other drug use disorders (e.g., methamphetamine, cocaine) were 1.55 and 2.33 times more likely to use ED or to be hospitalized

compared to those who used heroin only respectively (OR=1.55, 95%CI=1.49-1.60) (OR=2.33, 95%CI=1.30-4.21). In two studies out of 32 (Frank et al., 2015; John et al., 2017) and three studies (Choi et al., 2016; John et al., 2017; Laine et al., 2001), patients with SRDs who had alcohol use disorders were 1.12 and 1.55 times more likely to use ED or to be hospitalized compared to those who used cannabis respectively (OR=1.12, 95%CI=1.01-1.25) (OR=1.55, 95%CI=1.18-2.05) (**Figures 6, 7**).

Other clinical characteristics associated with ED use and hospitalization among patients with SRDs

In eleven studies out of 32 (Adam et al., 2020; Campbell et al., 2017; Cederbaum et al., 2014; Choi et al., 2018; Clark et al., 2013; Frank et al., 2015; Indig et al., 2010; John et al., 2017; Parthasarathy et al., 2005; Perron et al., 2011; Turner et al., 2003) and eight studies out of 32 (Campbell et al., 2017; Cederbaum et al., 2014; Choi et al., 2016; Di Giovanni et al., 2020; Laine et al., 2001; Parthasarathy et al., 2005; Reddon et al., 2021; Turner et al., 2003) patients who had MHDs were 1.54 and 1.40 times more likely to report ED use and hospitalization compared to those who did not have MHDs respectively (OR = 1.54, 95%CI = 1.20-1.98) (OR = 1.40, 95%CI = 1.07-1.83). In seven studies out of 32 (Campbell et al., 2017; Cederbaum et al., 2014; Choi et al., 2018; Larson et al., 2006; Parthasarathy et al., 2005; Siegal et al., 2006; Turner et al., 2003) and nine studies out of 32 (Binswanger et al., 2008; Campbell et al., 2017; Cederbaum et al., 2014; Laine et al., 2001; Mejia de Grubb et al., 2020; Parthasarathy et al., 2005; Stein et al., 2003; Turner et al., 2003; Walley et al., 2012) those who had chronic physical illnesses were 1.33 and 1.30 times more likely to have ED use or hospitalization compared to those who did not have chronic physical illnesses respectively (OR=1.33, 95%CI=1.15-1.54) (OR=1.30, 95%CI=1.15-1.47) (**Figures 6, 7**).

Figures 6, 7 here

Subgroup analyses

In the present study, several subgroup analyses were performed to investigate the main source of heterogeneity on pooled prevalence rates of ED use and hospitalization. Subgroup analyses were based on year of study publication, country, participants' sample size, type of drugs, diagnostic criteria for SRDs, and main reasons for ED use and hospitalization were run. However, no heterogeneity was detected regarding any of these variables (**Supplementary Files 3–14**).

Sensitivity analysis

Sensitivity analysis and Baujat plots were performed to assess influential effects. Effects on the right-hand side indicate studies with more heterogeneity. The studies that had the most contributions to the heterogeneity were removed following the sensitivity analysis. Although selectivity analysis was performed for each variable which had high heterogeneity, the sensitivity analysis did not decrease the heterogeneity between studies for some of the variables (e.g., being male, alcohol use disorder, MHDs, chronic physical illnesses) (**Supplementary Files 15–38**).

Publication bias

To identify probable publication bias, the Egger's and Begg's tests and their graphical representation were performed. Considering the symmetry assumption, no significant publication bias was observed in the reviewed studies selected for inclusion. As regards to the funnel plot, the paper distribution was not oriented in any specific direction, and for most of them, it was identical, confirming no publication biases in the present study (**Supplementary Files 39–50**).

Discussion

The present meta-analysis identified sociodemographic, types of drug and other clinical characteristics associated with ED use and hospitalization among patients with SRDs. Patients with SRDs who were the most at risk of being both ED users and hospitalized were those (i) having insurance, (ii) having other drugs and alcohol use disorders, (iii) having MHDs, and (iv) having chronic physical illnesses. The pooled prevalence rates of ED use and hospitalization in the present study were 36% and 41%, respectively. No pooled prevalence rate for ED use and hospitalization have previously been reported in relation to patients with SRDs.

The finding that patients with SRDs who have medical insurance were more likely to use ED or be hospitalized were found in previous studies (Cronquist et al., 2001; Rockett et al., 2003). A possible explanation for this results could be the fact that having medical insurance may increase access to health care (Card et al., 2008) and may increase use of ED and hospitalization (Zhou et al., 2017). That patients with lower educational were showed to use more ED is inconsistent with previous studies (Cederbaum et al., 2014; Chen et al., 2015). The admission rate was higher among patients with SRDs who have primary education attainment, compared to their counterparts who completed high school. This may be because patients with SRDs who had lower levels of education had also low economic status and lived in deprived areas, therefore they may have more complex conditions and need to use ED.

In line with previous studies, there was an association between alcohol and other drug use disorders and an enhanced risk for ED use and hospitalization among patients with SRDs (Armoon, Grenier, et al., 2021; Fleury et al., 2022). The studies highlighted that the main abused substances among patients with SRDs included alcohol (Wu et al., 2012) and cannabis (Campbell et al., 2017). The odds of requiring acute medical care services are higher in this population (Matson et al., 2020; Phillips et al., 2022). Consistent with the findings of research on early hospital readmission

(Armoon, Grenier, et al., 2021), it was found that patients with alcohol use disorders accounted for a large proportion of total cases of ED use and hospitalization, in comparison to other SRD groups. This finding could be understood in the context of the increased odds of experiencing chronic physical illnesses, such as liver diseases and cardiovascular disease (Cargiulo, 2007), a higher proneness to healthcare seeking, and episodes of alcohol withdrawal (Gupta et al., 2019) among alcohol use disorders patients, compared to patients with other SRD groups (Weisner et al., 2001).

Previous studies reported the association between ED use or hospitalization and having other drug use disorders (e.g., methamphetamine and cocaine) compared to those who used heroin only (Hendrickson et al., 2008; Marshall et al., 2012) which may be due to the serious negative effects of other drug use disorders such as methamphetamine on psychological functioning, which explains ED use (Sommers et al., 2006). ED use may be justified by the lack of availability of other outpatient services or adequate outpatient treatments for patients with SRDs who use methamphetamine (Hendrickson et al., 2008). Studies have reported a significant association of the odds of ED use or hospitalization with cocaine use (Miró et al., 2019; Sanvisens et al., 2021). A study reported a 18% readmission rate of ED user among cocaine users (Sanvisens et al., 2021), which may demonstrate the association of cocaine use and intense complications (Butler et al., 2017; Degenhardt et al., 2011). Also cocaine users may have higher risk of non-fatal and fatal overdose comparing to none cocaine users (Armoon, Mohammadi, et al., 2021; Armoon et al., 2022). Moreover, recreational cocaine use may cause accidents or misbehaviors that augment the likelihood of ED use (Fulde et al., 2015). Although, health care systems may screen and treat chronic medical conditions, more of these services may be required for patients with alcohol/other drug use disorders (Suen et al., 2022). Due to the lack of information for clinicians and limited capacity of inpatient health providers pharmacotherapies for alcohol/other drug use disorders and

referrals to specialty substance use treatment on discharge are not vastly practiced (Naeger et al., 2016; Rosenthal et al., 2016)

Our results supported previous findings indicating that the rate of using ED and hospitalization were significant among patients with SRDs who had MHDs (Armoon, Grenier, et al., 2021; Huynh et al., 2016; Vu et al., 2015). Moreover, this group tends to seek limited outpatient healthcare settings, attributable to their lack of or minimal tendency to adhere to medical care (Brorson et al., 2013; Coulson et al., 2009), explaining their high acute care use. The limitations of the availability of specialty treatment may also have led to high ED use and hospitalization (McCormack et al., 2015). The misunderstanding and negative attitudes toward patients with SRDs among some physicians may prevent them to identify SRDs as a conditions requiring outpatient treatment which justified ED use and hospitalization (Gilchrist et al., 2011; van Boekel et al., 2014). These patients searching care specially in ED have been reported rarely referred to specialists for treatment (Bogenschutz et al., 2014). In addition, individuals with SRDs and co-occurring MHDs or chronic physical disorders are more likely to have ED use since their complex conditions may not be properly managed in an outpatient health center (Huynh et al., 2016). Also, individuals with co-occurring SRDs and MHDs may search treatment for each of their condition separately since healthcare systems usually do not provide suitable integrated care (Lavergne et al., 2022).

Previous study reported that the rate of hospitalization was 58% among SRD patients with comorbid chronic physical illnesses (Binswanger et al., 2008). Additionally, the risk of experiencing co-occurring physical illnesses, including hypertension, diabetes, infective endocarditis, and cardiovascular disease has been found to be greater among those with SRDs,

leading to increased rates of ED use and hospitalization (Binswanger et al., 2008; Rudasill et al., 2019; Stein et al., 2003).

Limitations and strengths of the present study

This study has some limitations that should be acknowledged. First, some of the included studies utilized self-report survey to collect data. This data was thus subject to memory recall bias and social desirability bias. Second, some of the reviewed studies were based on cross-sectional research design, preventing the determination of causal and temporal correlations between the studied characteristics and acute care-seeking. Third, given the inclusion and exclusion criteria, there were no data concerning other essential features (e.g., primary care services use, non-fatal overdose, the duration of injection, the prevalence of cannabis use disorders, and employment status) that could have potentially impacted ED use and hospitalization. Fourth, there were limitations in the number of studies specifically examining a particular characteristic.

Sociodemographic characteristics associated with ED use or hospitalization were considered in 10 studies (31%), including four studies (12%) for being male, four (12%) and two studies (6%) for being of black ethnicity, seven (20%) and two (15%) studies for having health insurance, and four studies (12%) for lower educational level associated with ED use. Therefore, among sociodemographic characteristics there was high heterogeneity and the associations may be weak. There were also only a small number of studies considering sociodemographic characteristics, therefore the results should be interpreted with caution. Regarding type of drug use associated with ED use or hospitalization, there were four studies (12%) and four studies (12%) for other drug use disorders, and two studies (6%) and three studies (9%) for alcohol use disorder respectively. Therefore, among type of drug use, high heterogeneity was observed, which also

means that careful interpretation of the results is needed. Regarding clinical characteristics associated with ED use or hospitalization, there were eleven (34%) and nine studies (28%) for MHDs, and seven (22%) and nine studies (28%) for chronic physical illnesses, respectively. High heterogeneity was therefore observed among these variables, and the associations may be weak. Furthermore, due to low number of studies regarding clinical characteristics, caution must be taken when interpreting the results.

Finally, analysis indicated that the heterogeneity between studies was high in almost all variables. Several sensitivity analyses (e.g., year of study publication, country, participants' sample size, type of drugs, diagnostic criteria for SRDs) were tested but no sources of heterogeneity were found. However, the present study had a number of strengths, including the inclusion of a range of ED use and hospitalization associated variables. Additionally, major databases were searched, and the study employed a comprehensive search strategy. Moreover, the study reviewed a considerable number of papers meeting the inclusion/exclusion criteria which was a major advantage of the systematic review.

Conclusion

The findings showed that key sociodemographic and clinical characteristics including type of drug use were associated with ED use or hospitalization, the most important having other drugs and alcohol use disorders and having a MHD. Also, the frequency of ED use and hospitalization was greater among patients with co-occurring SRDs, MHDs, and chronic medical conditions. To improve treatment compliance and minimize ED use and hospitalization, implementation of comprehensive healthcare services is recommended comprising integrated SRD-MHD treatment and assertive community treatment for patients with SRDs. Interventions including addiction consultation services in hospitals, training ED and hospital providers to consider pharmacotherapy

for alcohol/other drug use disorders for patient treatments, and supporting these patients via social services and referring them to specialty care after discharge are recommended. A useful plan to reinforce chronic care in this population, especially among lower-educated patients, could provide information on the available outreach interventions after discharge from acute care units or hospitals. Essentially, outpatient healthcare access can be facilitated by implementing outreach programs tailored to patients with SRDs who have a lower level of education or low socioeconomic status.

Abbreviations

CI: Confidence interval

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

SRDs: Substance-related disorders

MHDs: Mental health disorders

WHO: World Health Organization

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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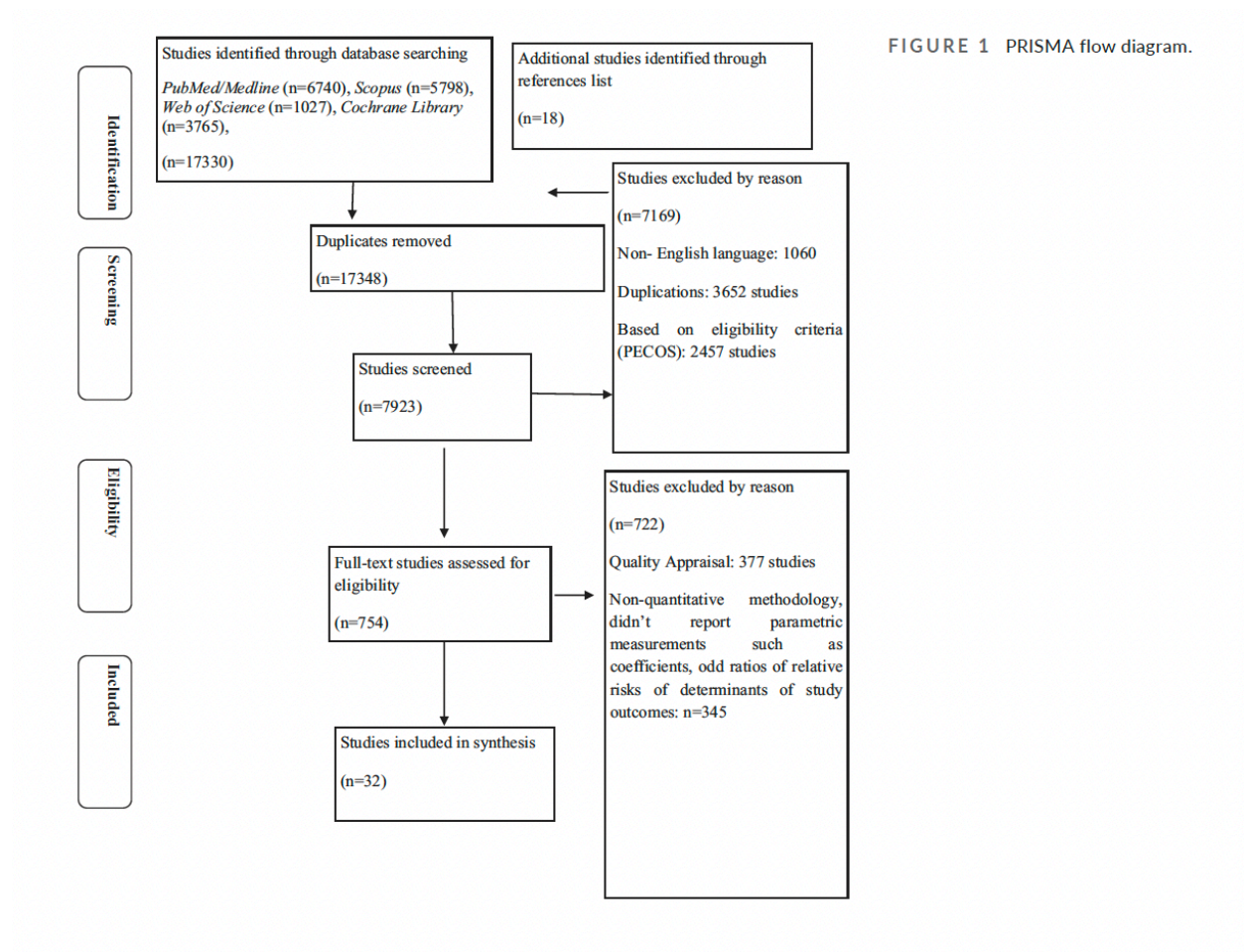
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Tables and figure legends:

TABLE 1 Studies' characteristics concerning emergency department (ED) use and hospitalization among patients with substance-related disorders.

ED use and hospitalization studies	Author (year of publication)	Years (y.) of data collections (number)	Sample at baseline	Final sample size (response rates)	Country	Study Design	Diagnostic criteria for substance-related disorders	Mean age (in years)	Male %	Female %
ED use studies (n=16)	Zhang et al. (2021)	2016–17 (2 y.)	27,609	27,609 (100%)	USA	CS ^a	ICD-10-CM ^c	46.5	44	56
	Adam et al. (2020)	2006–07 and 2013 (3 y.)	778	630 (81%)	Swaziland	CH ^b	ICD-10 ^d	24	66	34
	Manuel and Lee (2017)	2004–11 (8 y.)	14,245,776	14,245,776 (100%)	USA	CH ^b	ICD-9 ^e	36.5	58	42
	Choi et al. (2017)	2012–13 (2 y.)	14,715	14,715 (100%)	USA	CS ^a	DSM-5 ^f	63	47	53
	Ayangbayi et al. (2017)	2005–2011 (7 y.)	193,526	193,526 (100%)	USA	CS ^a	CDC/NCHS ^g	39.9	NR	NR
	Van Doren et al. (2016)	2010 (1 y.)	24,667	24,667 (100%)	USA	CS ^a	ICD-9-CM ^h	38.1	51	49
	Frank et al. (2015)	2008–13 (6 y.)	228,556	228,556 (100%)	USA	CS ^a	DSM-IV ⁱ	34	56	44
	Chen et al. (2015)	2007–08 (2 y.)	789	789 (100%)	Taiwan	CH ^b	DSM-IV ⁱ	34.7	87	13
	Clark et al. (2013)	2005–10 (6 y.)	1802	1178 (65%)	USA	CH ^b	ICD-9-CM ^h	47	82	18
	Wu et al. (2012)	2007–09 (3 y.)	113,673	113,673 (100%)	USA	CH ^b	DSM-IV ⁱ	41.5	45	55
	Perron et al. (2011)	2011 (1 y.)	43,093	43,093 (100%)	USA	CS ^a	DSM-IV ⁱ	36.5	61	39
	Hansagi et al. (2012)	2000–02 (3 y.)	1287	1287 (100%)	Sweden	CH ^b	ICD-10 ^d	50	72	28
	Indig et al. (2010)	2004–06 (3 y.)	263,937	245,975 (82%)	Australia	CS ^a	ICD-9 ^e	32.8	51	49
	Larson et al. (2006)	1997–99 (3 y.)	642	470 (73%)	USA	CS ^a	NR	35.8	75	25
	Siegal et al. (2006)	1996–97 (2 y.)	333	333 (100%)	USA	CS ^a	ICD-9-CM ^h	31	59	41
	Knowlton et al. (2005)	1994–96 (3 y.)	295	295 (100%)	USA	CS ^a	NR	43	66	34
Hospitalization studies (n=9)	Reddon et al. (2021)	2005–15 (11 y.)	1216	1216 (100%)	Canada	CH ^b	NR	21.8	69	31
	Di Giovanni et al. (2020)	2006–15 (10 y.)	2159	2159 (100%)	Italy	CS ^a	NR	38	80	20
	Mejia de Grubb et al. (2020)	2010–14 (5 y.)	118,000,000	118,000,000 (100%)	USA	CH ^b	ICD-9-CM ^h	49	57	43
	Choi et al. (2016)	2012 (1 y.)	115,656	115,656 (100%)	USA	CS ^a	ICD-9-CM ^h	57.6	67	33
	Walley et al. (2012)	2006–2008 (3 y.)	365	138 (38%)	USA	CS ^a	NR	47.8	65	35
	McDonald et al. (2011)	1995–2006 (12 y.)	41,062	41,062 (100%)	UK	CH ^b	ICD-9 ^e	26.8	71	29
	Binswanger et al. (2008)	2004–2008 (5 y.)	211	156 (74%)	USA	CH ^b	AUDIT-C and ASI ^j	42	63	37
	Stein and Anderson (2003)	2001–2002 (2 y.)	472	472 (100%)	USA	CH ^b	DSM-III ^k	37	61	39
	Laine et al. (2001)	1996–97 (2 y.)	58,248	58,248 (100%)	USA	CH ^b	ICD-9 ^e	27.5	58	42

Type of drug use	Reason for ED use and hospitalization	Percentage of ED use / hospitalization		Sociodemographic determinants				Type of drug				Clinical determinants	
				Being men	Black ethnicity	Lower level of education	Having insurance	Heroin use disorders	Alcohol use disorders	Other drug use disorders	Opioid use disorders	Mental disorders	Chronic physical illnesses
Polysubstance use	Any reason	11.9	-	*			*						
Alcohol use	Any reason	60	-									*	
Polysubstance use	Substance use	NA	-							*			
Cannabis use	Any reason	30.9	-				*					*	*
Polysubstance use	Any reason	NA	-		*		*						
Polysubstance use	Any reason	24.3	-	*									
Polysubstance use	Any reason	NA	-	*	*		*		*	*		*	
Heroin use	Any reason	19.5	-			*				*			
Alcohol use	Any reason	38	-									*	
Polysubstance use	Any reason	27.8	-	*		*							
Polysubstance use	Any reason	3.7	-									*	
Polysubstance use	Substance use	21	-					*					
Polysubstance use	Any reason	NA	-									*	
Polysubstance use	Any reason	47	-				*						*
Cocaine use	Any reason	67.52	-	*									*
Polysubstance use	Injection drug user	14	-				*						
Cannabis use	Cannabis use	-	NA									*	
Polysubstance use	Any reason	-	NA								*	*	
Polysubstance use	Any reason	-	NA				*				*		*
Polysubstance use	HIV infection	-	NA						*	*		*	
Polysubstance use	Methadone use	-	58										*
Polysubstance use	Alcohol use reason	-	8.1	*									
Polysubstance use	Soft tissue infection	-	55										*
Heroin and cocaine	Any reason	-	13.4										*
Polysubstance use	Illicit drug	-	NA						*			*	*

TABLE 1 Continued

ED use and hospitalization studies	Author (year of publication)	Years (y.) of data collections (number)	Sample at baseline	Final sample size (response rates)	Country	Study Design	Diagnostic criteria for substance-related disorders	Mean age (in years)	Male %	Female %
ED use and hospitalization (n=7)	John and Wu (2017)	2005–13 (9 y.)	16,757	16,757 (100%)	USA	CS ^a	DSM-IV ⁱ	31	67	33
	Campbell et al. (2017)	2010–14 (5 y.)	2752	2757 (100%)	USA	CH ^b	ICD-9 ^c	36.4	64	36
	Cederbaum et al. (2014)	2006–09 (4 y.)	73,251	73,251 (100%)	USA	CS ^a	NR	39.8	65	35
	Rockett et al. (2005)	1996–97 (2 y.)	1890	1502 (79%)	USA	CS ^a	DSM-IV ⁱ	41.5	56	44
	Parthasarathy and Weisner (2005)	1994–96 (3 y.)	1204	1204 (100%)	USA	CH ^b	DSM-IV ⁱ	38.4	NR	NR
	Turner et al. (2003)	1996–97 (2 y.)	11,556	11,556 (100%)	USA	CH ^b	ICD-9-CM ^h	NR	NR	NR
	Palepu et al. (1999)	2001 (1 y.)	1103	1103 (100%)	Canada	CH ^b	NR	35	65	35

^aCross-sectional study.^bCohort study.^cInternational Classification of Diseases, Tenth Revision Clinical Modification.^dInternational Classification of Diseases, Tenth Revision.^eInternational Classification of Diseases, Ninth Revision.^fDiagnostic and Statistical Manual of Mental Disorders, Fifth Edition.^gThe Centers for Disease Control and Prevention's National Center for Health Statistics.^hInternational Classification of Diseases, Ninth Revision Clinical Modification.ⁱDiagnostic and Statistical Manual of Mental Disorders, Fourth Edition.^jAlcohol Use Disorders Identification Test-consumption and Addiction Severity Index.^kDiagnostic and Statistical Manual of Mental Disorders, Third Edition.

*Variables that are included in the meta-analysis.

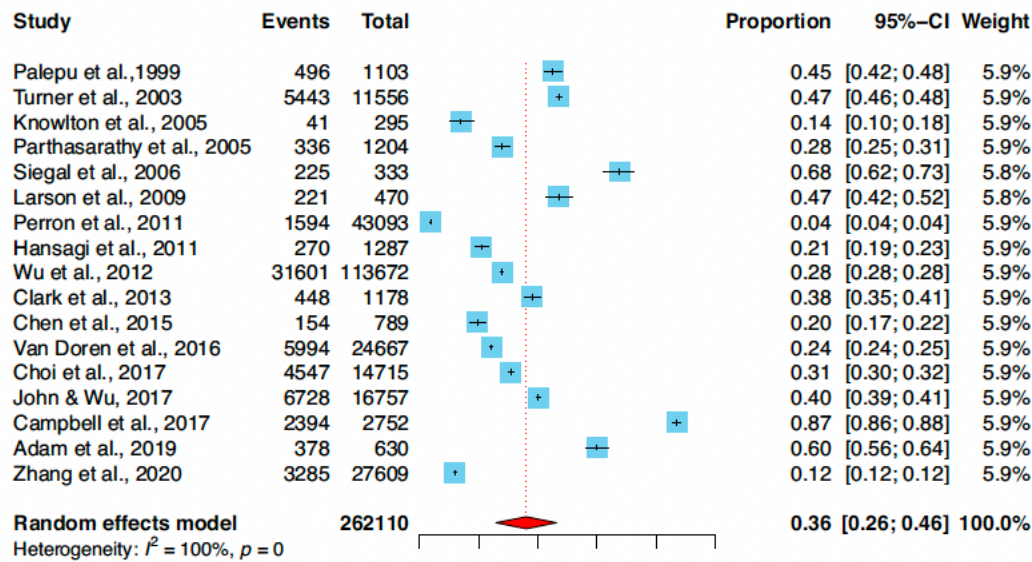


FIGURE 2 The pooled prevalence rate of emergency department use among substance-related disorders.

Type of drug use	Reason for ED use and hospitalization	Percentage of ED use / hospitalization	Sociodemographic determinants				Type of drug				Clinical determinants	
			Being men	Black ethnicity	Lower level of education	Having insurance	Heroin use disorders	Alcohol use disorders	Other drug use disorders	Opioid use disorders	Mental disorders	Chronic physical illnesses
Cannabis use	Any reason	40.15	10.04	*				*	*		*	
Cannabis use	Any reason	87	76	*	*						*	*
Polysubstance use	Any reason	NA	NA	*	*		*		*		*	*
Polysubstance use	Any reason	NA	NA			*						
Polysubstance use	Drug use reason	27.89	15.84								*	*
Polysubstance use	HIV infection	47.1	93.1								*	*
Heroin and cocaine	Any reason	45	21	*								

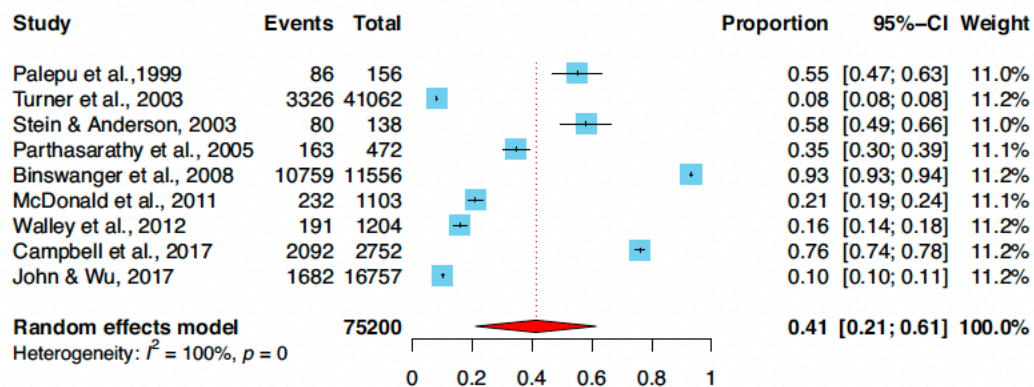


FIGURE 3 The pooled prevalence rate of hospitalization among substance-related disorders.

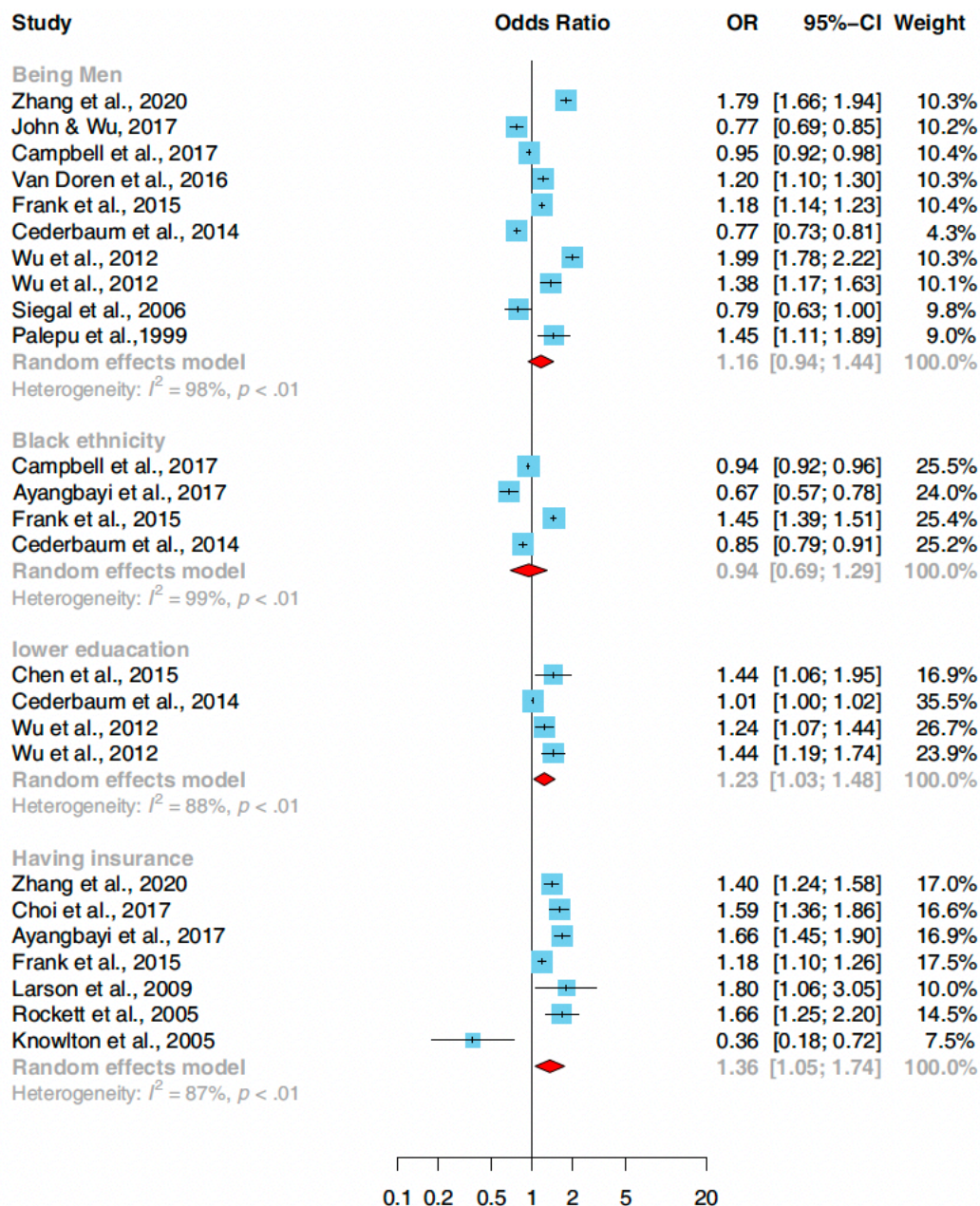


FIGURE 4 Pooled odds ratio of sociodemographic characteristics associated with emergency department use among substance-related disorders.

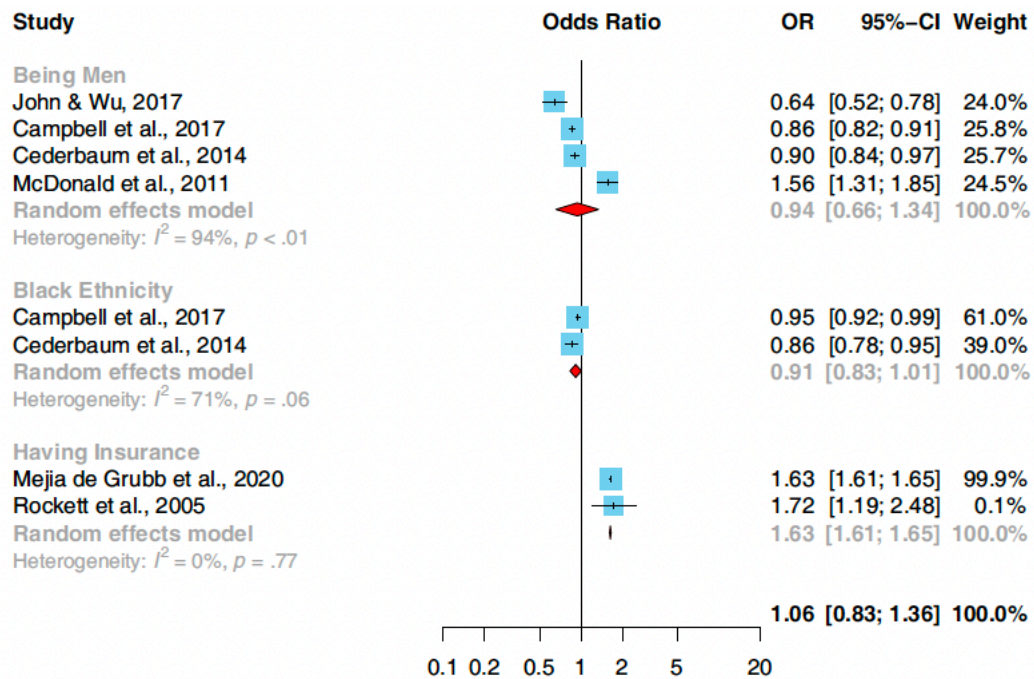


FIGURE 5 Pooled odds ratio of sociodemographic characteristics associated with hospitalization among substance-related disorders.

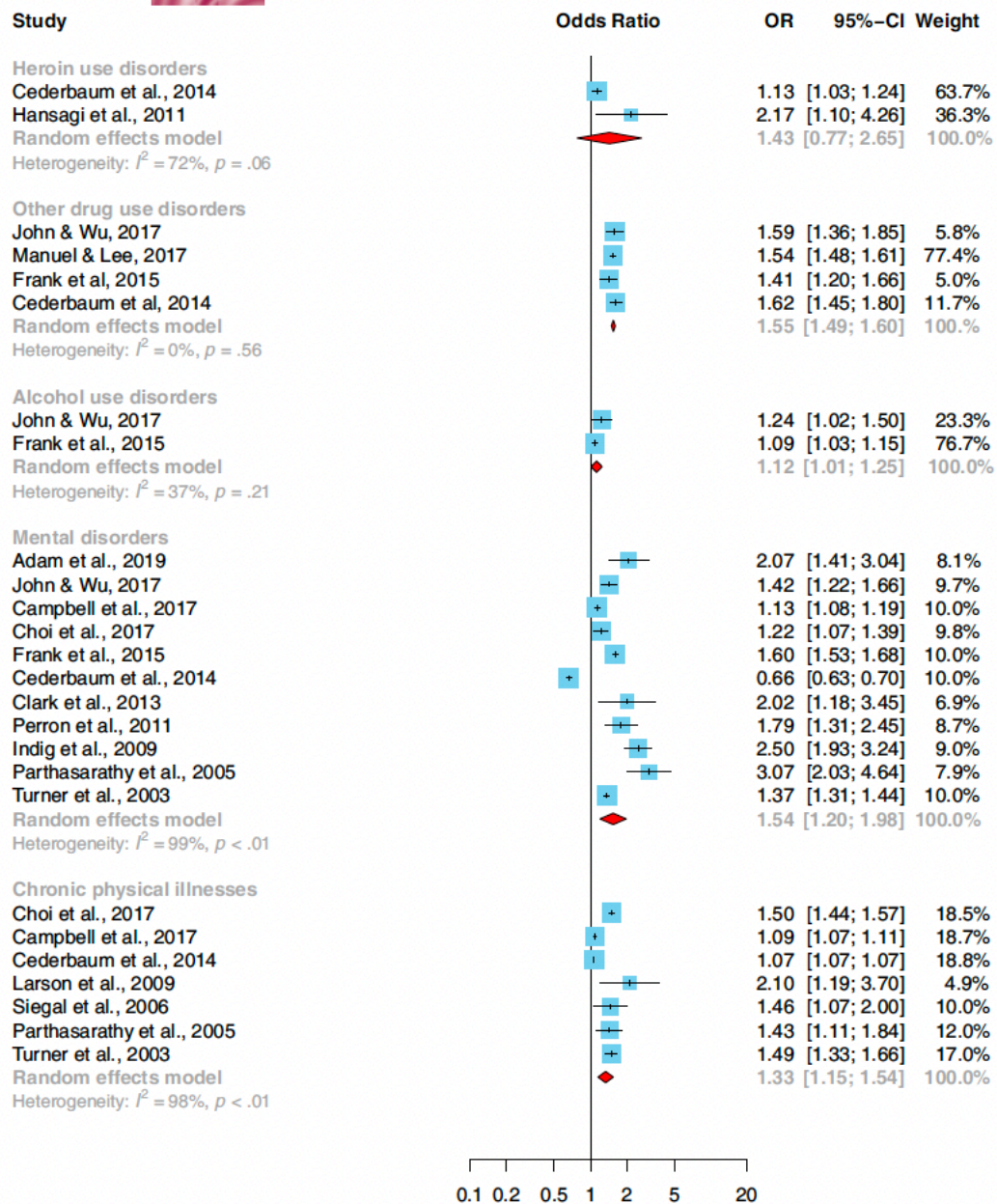


FIGURE 6 Pooled odds ratio of type of drug and clinical determinants associated with emergency department use among substance-related disorders.

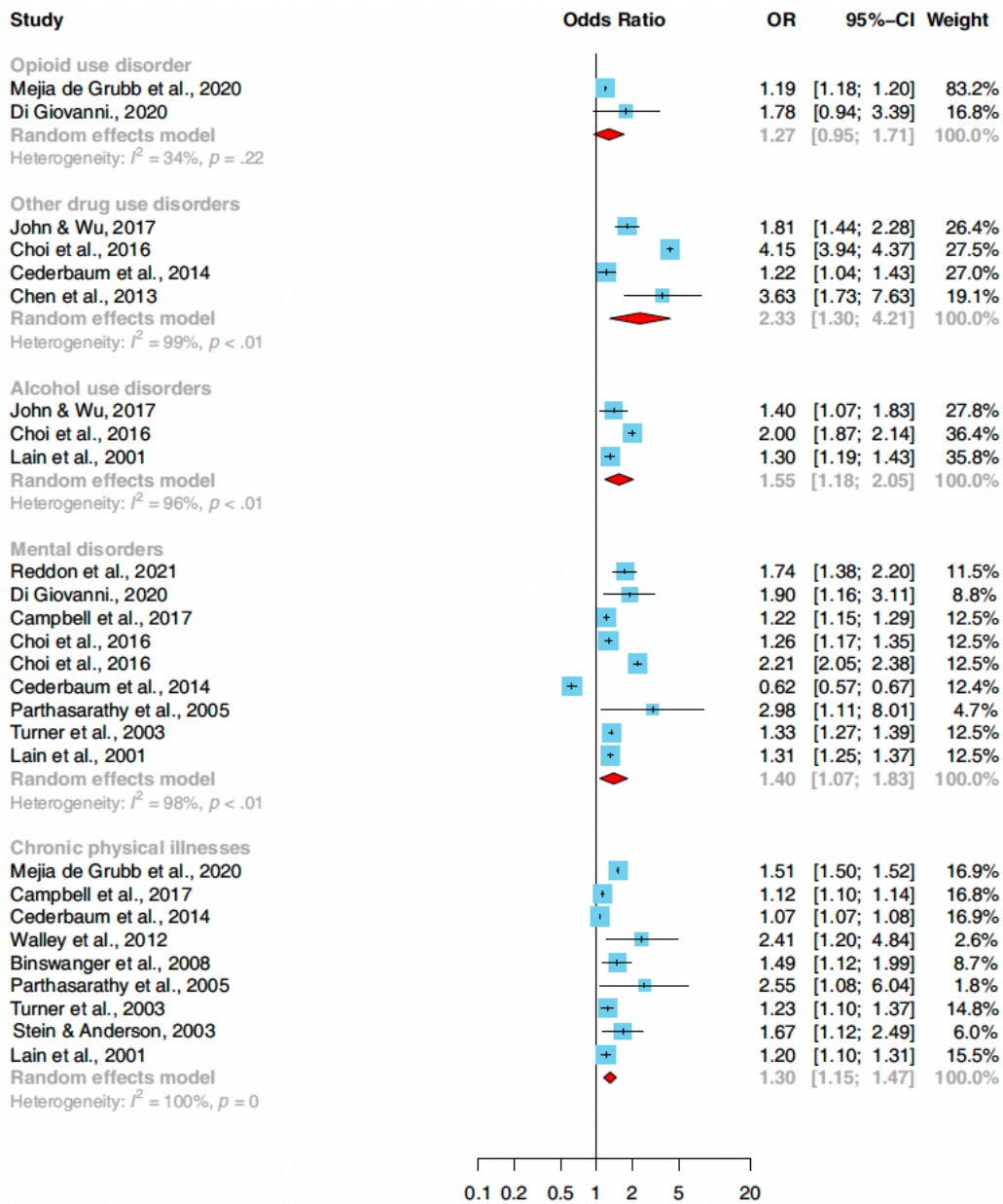


FIGURE 7 Pooled odds ratio of type of drug and clinical determinants associated with hospitalization among substance-related disorders.

Table 1. Studies characteristics on emergency department (ED) use and hospitalization among patients with substance-related disorders

Figure 1. PRISMA flow diagram

Figure 2. The pooled prevalence rate of emergency department use among substance-related disorders.

Figure 3. The pooled prevalence rate of hospitalization among substance-related disorders.

Figure 4. Pooled odds ratio of sociodemographic characteristics associated with emergency department use among substance-related disorders.

Figure 5. Pooled odds ratio of sociodemographic characteristics associated with hospitalization among substance-related disorders.

Figure 6. Pooled odds ratio of type of drug and clinical determinants associated with emergency department use among substance-related disorders.

Figure 7. Pooled odds ratio of type of drug and clinical determinants associated with hospitalization among substance-related disorders.

Supplementary File 1. Search strategy

Supplementary File 2. Risk of bias assessment using the Newcastle-Ottawa Scale

Supplementary File 3. Subgroup analysis based on year of publication of studies for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 4. Subgroup analysis based on year of publication of studies for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 5. Subgroup analysis based on country for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 6. Subgroup analysis based on country for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 7. Subgroup analysis based on participants' sample size for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 8. Subgroup analysis based on participants' sample size for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 9. Subgroup analysis based on type of drugs for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 10. Subgroup analysis based on type of drugs for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 11. Subgroup analysis based on diagnostic criteria used for SRD for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 12. Subgroup analysis based on diagnostic criteria used for SRD for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 13. Subgroup analysis based on main reason for the pooled prevalence rate of emergency department use among substance-related disorders.

Supplementary File 14. Subgroup analysis based on main reason for the pooled prevalence rate of hospitalization among substance-related disorders.

Supplementary File 15. Baujat plot for being male associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 16. Pooled odds ratio of being male associated with emergency department use after removing Zhang et al (2020) and Cederbaum et al (2014) (studies that had the most contribution of heterogeneity)

Supplementary File 17. Baujat plot for being male associated with hospitalization. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 18. Pooled odds ratio of being male associated with hospitalization after removing McDonald et al., 2011 (study that had the most contribution of heterogeneity)

Supplementary File 19. Baujat plot for being Black ethnicity associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 20. Pooled odds ratio of being Black ethnicity associated with emergency department use after removing Frank et al (2015) (study that had the most contribution of heterogeneity)

Supplementary File 21. Baujat plot for lower educational level associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 22. Pooled odds ratio of lower educational level associated with emergency department use after removing Wu et al (2012) (study that had the most contribution of heterogeneity)

Supplementary File 23. Baujat plot for having insurance associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 24. Pooled odds ratio of having insurance associated with emergency department use after removing Knowlton et al (2005), Ayangbayi et al (2017) and Frank et al (2015) (studies that had the most contribution of heterogeneity)

Supplementary File 25. Baujat plot for having other drug use disorders associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 26. Pooled odds ratio of having other drug use disorders associated with emergency department use after removing Frank et al (2015) (study that had the most contribution of heterogeneity)

Supplementary File 27. Baujat plot for having other drug use disorders associated with hospitalization. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 28. Pooled odds ratio of having other drug use disorders associated with hospitalization after removing Cederbaum et al., 2014 (study that had the most contribution of heterogeneity)

Supplementary File 29. Baujat plot for having alcohol use disorders associated with hospitalization. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 30. Pooled odds ratio of having alcohol use disorders associated with hospitalization after removing Lain et al., 2001 (study that had the most contribution of heterogeneity)

Supplementary File 31. Baujat plot for having mental health disorders associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 32. Pooled odds ratio of having mental health disorders associated with emergency department use after removing Cederbaum et al (2014) (study that had the most contribution of heterogeneity)

Supplementary File 33. Baujat plot for having mental health disorders associated with hospitalization. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 34. Pooled odds ratio of having mental health disorders associated with hospitalization after removing Cederbaum et al., 2014 (study that had the most contribution of heterogeneity)

Supplementary File 35. Baujat plot for having chronic physical illnesses associated with emergency department use. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 36. Pooled odds ratio of having chronic physical illnesses associated with emergency department use after removing Choi et al (2017) (study that had the most contribution of heterogeneity)

Supplementary File 37. Baujat plot for having chronic physical illnesses associated with hospitalization. Effects on the right part indicated studies contribute much to the heterogeneity

Supplementary File 38. Pooled odds ratio of having chronic physical illnesses associated with hospitalization after removing Mejia de Grubb et al., 2020 (study that had the most contribution of heterogeneity)

Supplementary File 39. Publication bias for being male associated with emergency department use

Supplementary File 40. Publication bias for being Black ethnicity associated with emergency department use

Supplementary File 41. Publication bias for having lower educational level associated with emergency department use

Supplementary File 42. Publication bias for having insurance associated with emergency department use

Supplementary File 43. Publication bias for having other drug use disorders associated with emergency department use

Supplementary File 44. Publication bias for having mental disorders associated with emergency department use

Supplementary File 45. Publication bias for having chronic physical illnesses associated with emergency department use

Supplementary File 46. Publication bias for being male associated with hospitalization

Supplementary File 47. Publication bias for having other drug use disorders associated with hospitalization

Supplementary File 48. Publication bias for having alcohol use disorders associated with hospitalization

Supplementary File 49. Publication bias for having mental disorders associated with hospitalization

Supplementary File 50. Publication bias for having chronic physical illnesses associated with hospitalization

