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Substance use disorder and risk of suicidal ideation, suicide attempt and suicide death: a meta-analysis

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ABSTRACT

Background This meta-analysis addressed the association between substance use disorder (SUD) and suicide outcomes based on current evidence.

Methods We searched PubMed, Web of Science and Scopus until May 2015. We also searched the reference lists of included studies and Psycinfo website. We included observational (cohort, case–control, cross-sectional) studies addressing the association between SUD and suicide. Our outcomes of interest were suicide ideation, suicide attempt and suicide death. For each outcome, we calculated the odds ratio (OR) or risk ratio (RR) with 95% confidence intervals (CI) based on the random-effects model.

Results We identified a total of 12 413 references and included 43 studies with 870 967 participants. There was a significant association between SUD and suicidal ideation: OR 2.04 (95% CI: 1.59, 2.50; $I^2 = 88.8\%$, 16 studies); suicide attempt OR 2.49 (95% CI: 2.00, 2.98; $I^2 = 94.3\%$, 24 studies) and suicide death OR 1.49 (95% CI: 0.97, 2.00; $I^2 = 82.7\%$, 7 studies).

Conclusions Based on current evidence, there is a strong association between SUD and suicide outcomes. However, evidence based on long-term prospective cohort studies is limited and needs further investigation. Moreover, further evidence is required to assess and compare the association between suicide outcomes and different types of illicit drugs, dose–response relationship and the way they are used.

Keywords meta-analysis, self-injurious behavior, self-mutilation, substance-related disorders, suicide

Introduction

Suicide is a serious public health problem with long-term harmful effects on individuals, families and communities.[1] Every year, >800 000 people die by suicide, that is one death due to suicide every 40 s.[2,3] For every suicide death, there are between 10 and 40 attempted suicides.[4] Suicide accounted for 1.4% of all deaths worldwide, making it the 15th leading cause of death globally and the second leading cause of death among people aged 15–29 years in 2012.[2] In fact, suicide is among the greatest sources of premature death.[5]

Suicide is associated with several risk factors, including psychiatric disorders, drug misuse, psychological states, genetics, cultural and social situations.[6–8] Other risk factors include having previously attempted suicide,[4] alcohol and drug abuse.[9–11] About 230 million people, or 5% of the world's adult population, aged 15–64, are estimated to have used an illicit drug at least once.[12]

Several epidemiological studies have evaluated the role of illicit drug use in suicide behaviors. However, the results of these studies are generally inconsistent. On the other hand, several reviews[13,14] and a few meta-analyses[15,16] have addressed this issue, but they are either out-of-date or limited to suicide death[15] or investigated the relationship between suicide and co-occurring mental disorders and illicit drug misuse.[16] Therefore, this meta-analysis was conducted to address the association between substance use disorder (SUD) and suicidal ideation, suicide attempt and suicide death based on current evidence.

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Materials and methods

Criteria for including studies

Observational (cohort, case–control and cross-sectional) studies addressing the association between suicide and SUD were included irrespective of language, age, gender, nationality, religion, race or publication status (full text or abstract). The observational studies that described the suicide rate among substance abusers without control group were excluded.

The exposure of interest was SUD, including substance abuse and substance dependence, refers to the frequent use of, or dependence on, a drug leading to effects that are detrimental to the individual's physical and mental health.[17] In cases where multiple substances were included in a study for analysis, we used the combined effect of the substances in the meta-analysis and the individual effect of each substance for subgroup analysis. The studies that did not distinguish alcohol use disorder from SUD and their combined effect were excluded.

The outcomes of interest were suicide ideation, suicide attempt and suicide death. The suicidal ideation is 'thinking about, considering or planning for suicide'.[18] The suicide attempt is 'a non-fatal, self-directed potentially injurious behavior with any intent to die as a result of the behavior'.[18] The suicide death is 'a death caused by self-directed injurious behavior with any intent to die as a result of the behavior'.[18] The death due to overdose without intent to die was not included. The studies that reported suicide outcomes (ideation, attempt and death) as a whole were excluded.

Search methods

The following MeSH terms as well as conventional terms were used: (suicide or self-injurious behavior or self-mutilation or self-immolation or self-harm or self-inflicted or self-injury) and (opioid or opium or narcotic or opiate or substance or drug or chemical or addict or addiction) and (cohort stud* or follow-up stud* or longitudinal stud* or case–control stud* or case-base stud* or cross-sectional stud* or observational stud* or survey).

Major international electronic databases (PubMed, Web of Science and Scopus) were searched until May 2015. In addition, the reference lists of the included studies and Psycinfo web site were searched for additional studies.

Data collection and analysis

Two authors (J.P. and N.D.) independently assessed their fulfillment of the inclusion criteria. Disagreements were resolved by discussion until consensus was reached. Then, the full texts of the eligible studies were reviewed and the following data were extracted: first author's name, year of publication, country where the study was conducted, age and gender of participants, study design, length of follow-up (for cohort studies), types of suicide outcomes (ideation, attempt and death) and types of substances (cannabis, tranquilizers, cocaine, marijuana, amphetamine, opioid, steroid, inhalants, hallucinogen and ecstasy), adjusting for confounders, sample size, effect estimate and its 95% confidence interval (CI).

The quality of reporting and the risk of bias of the included studies were explored using Newcastle Ottawa Statement (NOS) Manual.[19] The NOS scale provides a checklist of items for judging the risk of bias in the included studies and allocates a maximum of nine stars to the following domains: selection, comparability, exposure and outcome. In this review, the studies with seven star items or more were considered high quality, and those with six star items or less were considered low quality based on our own experience.[11,20,21]

Heterogeneity was explored by Q-test,[22] and the quantity of heterogeneity was measured by I^2 statistic.[23] Publication bias was assessed using the Egger's[24] and Begg's[25] tests.

Risk ratio (RR) and odds ratio (OR) with their 95% CIs were expressed as measures of association between SUD and suicide outcomes. Wherever possible, we used the full adjusted forms of RR and OR controlled for at least one or more of the potential confounding factors such as psychiatric disorder, alcohol use disorder, age, gender, ethnicity, educational level, marital status, income, smoking and history of suicide. Data were analyzed, and the results were reported by suicide outcomes (ideation, attempt and death) using a random-effects model.[26] Subgroup analysis was performed based on types of substance and adjusting for different confounders. In addition, a meta-regression was performed to explore sources of heterogeneity. All statistical analyses were performed at a significance level of 0.05 using Stata software, version 11 (StataCorp, College Station, TX, USA).

Results

Results of the search

We identified a total of 12 413 references through searching the electronic searches until May 2015 and screening the reference lists. We excluded 4023 duplicates and 8275 irrelevant references through reading titles and abstracts. Accordingly, 115 references were retrieved for further assessment. We excluded 72 references, because they were not original article (i.e. letter, commentary, review) or they did not meet our inclusion criteria. Finally, 43 references fulfilled the inclusion criteria (Fig. 1), including 12 cohort studies, 10 case–control studies and 21 cross-sectional studies involving 870 967 participants (Table 1). Seventeen studies addressed suicidal ideation,[27–43]

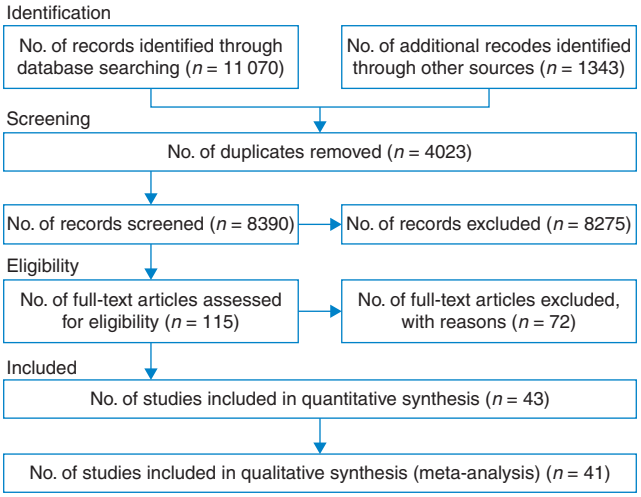

Fig. 1 Flow of information through the different phases of the systematic review.

29 studies addressed suicide attempt,[27,28,32–34,36–40,42–60] and 10 studies addressed suicide death.[8,59,61–67] Thirteen studies[27,28,32–34,36–40,42,43,59] have reported the association between SUD and different types of suicide (ideation, attempts and death) in separate; therefore, the number of studies presented in the forest plots is more than the number of included studies. Forty studies were published in English, one in Spanish,[66] one in French[58] and one in Korea.[53]

Effects of exposure

The associations between SUD and suicide outcomes are given in Figs 2–4. According to Fig. 2, SUD was associated with an increased risk of suicide ideation: OR 2.53 (95% CI: 1.67, 3.39; $I^2 = 90.1\%$, 9 studies) based on low-quality studies and OR 1.37 (95% CI: 0.98, 1.75; $I^2 = 68.5\%$, 7 studies) based on high-quality studies. According to a single cohort study[39] (not shown in the figure), the RR estimate of suicidal ideation in drug abusers compared with non-users was 1.85 (95% CI: 1.36, 2.52).

According to Fig. 3, SUD was associated with an increased risk of suicide attempt: OR 2.88 (95% CI: 2.02, 3.74; $I^2 = 93.4\%$, 15 studies) based on low-quality studies and OR 1.80 (95% CI: 1.30, 2.29; $I^2 = 84.6\%$, 9 studies) based on high-quality studies. According to three cohort studies (not shown in the figure), the RR estimate of suicide attempt in drug abusers compared with non-users was 2.52 (95% CI: 1.82, 3.22; $I^2 = 36.2\%$, 3 studies).

According to Fig. 4, SUD was associated with an increased risk of suicide death: OR 1.54 (95% CI: 0.81, 2.28; $I^2 = 74.1\%$, 4 studies) and RR 1.44 (95% CI: 0.67, 2.21; $I^2 = 74.0\%$, 3 studies).

There were two outliers (not shown in the figure) that reported an extremely high association between SUD and suicide death. One of them was a cross-section study[8] that reported that the OR estimate of suicide death among drug abusers versus non-users was 7.23 (95% CI: 5.57, 9.39) and the other one was a cohort study[64] that reported that the hazard ratio of suicide death among drug abusers versus non-users was 10.78 (95% CI: 6.05, 19.21).

Publication bias

Publication bias was assessed using Begg's and Egger's tests. Based on these statistical tests, there was no evidence of publication bias among studies addressing the association between SUD and suicidal ideation ($P = 0.857$ and $P = 0.265$), suicide attempt ($P = 0.843$ and $P = 0.506$) and suicide death ($P = 1.000$ and $P = 0.500$), respectively.

Quality of the studies

The quality of reporting and the risk of bias of the included studies were explored using NOS scale. According to this scale, 23 studies were of low quality and 20 studies were of high quality. We presented the results of meta-analysis by the quality of the studies.

Subgroup analysis

So as to explore the source of heterogeneity, we performed subgroup analysis based on the types of substances and adjusting for different confounders (Table 2). We did not perform subgroup analysis for the participants' age, because the range of age was too wide across studies. There were a limited number of studies that reported SUD and suicide relationship by gender. Therefore, it was impossible to perform a robust meta-analysis to estimate the risk of suicide by gender.

The effect of opioid on suicidal ideation and attempt was stronger than other substances and the effect of cannabis was weaker than others, although the results were not very different. There was no enough evidence to assess and compare the effect of different substances on suicide death. The adjusted estimates of ORs of suicidal ideation and death were much greater than unadjusted ones, whereas this issue was the opposite to that of suicide attempt.

We performed a meta-regression to explore the sources of heterogeneity across studies (Table 3). We considered suicide as outcome and covariates such as types of substance, adjusting for different confounders, sex ratio and mean age as predictors. The results of meta-regression provided useful information about the effect of different covariates on suicide outcomes, although their results were not statistically significant.

Table 1 Summary of studies results

First author, year	Country	Age mean	Sex	Population	Design	Follow-up (years)	Substance abuse	Suicide			Adjustment	Effect size	Sample size	NOS score	Quality
								I	A	D					
Adams, 1992	USA	33.70	Both	Psychiatric	Case–Control	0	Drug	✓	✓		Crude	Odds ratio	649	★★★★★	Low
Allebeck, 1990	Sweden	18–20	Male	Conscripts	Cohort	14	Drug			✓	Crude	Odds ratio	50 465	★★★★★★★	High
Allgulander, 1992	Sweden	18+	Both	Psychiatric	Cohort	15	Drug			✓	Al-Ps-Others	Risk ratio	80 970	★★★★★★★★	High
Arenliu, 2014	Albania	15.64	Both	General	Cross-sectional	0	Ca, Tr	✓	✓		Others	Odds ratio	4709	★★★★★	Low
Beautrais, 1999	New Zealand	18+	Both	General	Case–Control	0	Ca		✓		Al-Ps-Others	Odds ratio	1330	★★★★★★★★★	High
Borges, 2000	USA	15–54	Both	Psychiatric	Cross-sectional	0	Drug		✓		Al-Ps-Others	Odds ratio	5877	★★★★★★★★	High
Brent, 1993	USA	17.20	Both	General	Case–Control	0	Drug			✓	Crude	Odds ratio	134	★★★★★★★	High
Brezo, 2007	Canada	6–24	Both	General	Cohort	13	Drug		✓		Crude	Odds ratio	3017	★★★★★★	Low
Chan, 2013	Malaysia	17.68	Both	General	Cross-sectional	0	Drug	✓			Al-Others	Odds ratio	4581	★★★★★★	Low
Christiansen, 2009	Denmark	15+	Both	Psychiatric	Case–Control	0	Drug		✓		Al-Ps-Others	Risk ratio	63 332	★★★★★★★★★	High
Coelho, 2010	Brasil	18+	Both	General	Cross-sectional	0	Drug	✓			Crude	Odds ratio	1464	★★★★★★	Low
Dunlavy, 2015	Tanzania	11–16	Both	General	Cross-sectional	0	Drug	✓			Others	Odds ratio	2176	★★★★★	Low
Feodor, 2014	Denmark	16+	Both	General	Cohort	9	Drug			✓	Other	Hazard ratio	32 010	★★★★★★★★	High
Finley, 2015	USA	18–56	Both	Veterans	Cohort	3	Drug	✓	✓		Crude	Odds ratio	211 652	★★★★★	Low
Flensborg, 1999	Denmark	20–93	Both	General	Cohort	26	Drug			✓	Crude	Hazard ratio	18 146	★★★★★★	Low
Garrison, 1993	USA	14–18	Both	General	Cross-sectional	0	Drug, Co, Ma	✓	✓		Others	Odds ratio	3764	★★★★★	Low
Gmitrowicz, 2003	Poland	14–21	Both	General	Cross-sectional	0	Drug	✓	✓		Al-Ps-Others	Odds ratio	1663	★★★★★★★	High
Gonzalez, 2007	Spain	28.86	Both	Psychiatric	Cohort	5	Co, Am		✓		Ps-Others	Odds ratio	83	★★★★★	Low
Hallfors, 2004	USA	16.30	Both	General	Cross-sectional	0	Drug, Ma	✓			Others	Odds ratio	18 924	★★★★★★★	High
Kaslow, 2000	USA	30.80	Female	General	Case–Control	0	Drug		✓		Ps-Others	Odds ratio	285	★★★★★★★★	High
Kelly, 2002	USA	16.20	Both	Psychiatric	Case–Control	0	Ca, Co, Am		✓		Crude	Odds ratio	192	★★★★★	Low
Kelly, 2004	USA	12–19	Both	Psychiatric	Cross-sectional	0	Ca, Co, Op		✓		Others	Odds ratio	503	★★★★★★★	High
Kessler, 1999	USA	15–54	Both	General	Cross-sectional	0	Drug	✓	✓		Others	Odds ratio	5877	★★★★★★★★	Low
Kim, 2012	USA	50–70	Both	Psychiatric	Case–Control	0	Drug			✓	Crude	Odds ratio	636	★★★★★	Low
Kokkevi, 2012	Europe	15–16	Both	General	Cross-sectional	0	Ca, Drug		✓		Others	Odds ratio	43 664	★★★★★★	Low
Liu, 2014	USA	15.70	Both	Psychiatric	Cross-sectional	0	Co, Op, IDU	✓	✓		Ps-Others	Odds ratio	2095	★★★★★★★	High
Miller, 2011	Mexico	12–17	Both	General	Cross-sectional	0	Drug	✓	✓		Others	Odds ratio	3005	★★★★★★★★	High
Ocampo, 2009	Mexico	5–40	Both	General	Cross-sectional	0	Drug			✓	Crude	Odds ratio	98 434	★★★★★★★	High
Park, 2008	Korea	16.00	Both	General	Cross-sectional	0	Drug		✓		Crude	Odds ratio	71 404	★★★★★	Low
Pirkis, 2000	Australia	18+	Both	General	Cross-sectional	0	Drug	✓	✓		Others	Risk ratio	10 641	★★★★★★	Low
Poorolajal, 2015	Iran	25.30	Both	General	Cross-sectional	0	Drug			✓	Ps-Others	Odds ratio	13 810	★★★★★★★	High
Rasic, 2013	Canada	15.50	Both	General	Cohort	2	Ca	✓	✓		Al-Others	Odds ratio	976	★★★★★★★	High
Reutfors, 2009	Sweden	32.80	Both	Psychiatric	Case–Control	0	Ca			✓	Others	Odds ratio	168	★★★★★★★★	High
Reyes, 2011	Puerto Rico	12–15	Both	General	Cohort	1	Drug		✓		Crude	Odds ratio	691	★★★★★	Low
Rivlin, 2010	UK	18–50	Male	Prisoners	Case–Control	0	Drug		✓		Crude	Odds ratio	120	★★★★★★	Low

Roberts, 2010	USA	11–17	Both	General	Cohort	1	Ma	✓	Crude	Odds ratio	3134	★★★★★	Low
Robinson, 2009	Australia	15–29	Both	Psychiatric	Cohort	2	Ca	✓	Others	Odds ratio	661	★★★★★	Low
Rudatsikira, 2007	Zimbabwe	11–17	Both	General	Cross-sectional	0	Ca	✓	Crude	Odds ratio	1970	★★★★★	Low
Schaller, 1996	Switzerland	18–39	Both	Prisoners	Case–Control	0	Drug	✓	Others	Odds ratio	341	★★★★★★	Low
Simon, 2007	USA	38.40	Both	Psychiatric	Cohort	7	Drug	✓	Ps-Others	Hazard ratio	32 360	★★★★★★★	High
Ursoniu, 2009	Romania	16.79	Both	General	Cross-sectional	0	Drug	✓	Crude	Odds ratio	2908	★★★★★	Low
Wong, 2013	USA	12–18	Both	General	Cross-sectional	0	Co, Ma, Am, Op, St, In, Ec, Ha,	✓	Al-Ps-Others	Odds ratio	73 183	★★★★★★★	High
Wu, 2004	USA	9–17	Both	General	Cross-sectional	0	Drug	✓	Al-Ps-Others	Odds ratio	1458	★★★★★★★★	High

NOS, Newcastle Ottawa Statement score; Ca, Cannabis; Tr, Tranquilizers; Co, Cocaine; Ma, Marijuana; Am, Amphetamine; Op, Opioid; St, Steroid; In, Inhalants; Ha, Hallucinogen; Ec, Ecstasy; Al, Alcohol use disorder; Ps, Psychiatric disorder; Other, Other covariates such as age, gender, ethnicity, educational level, marital status, income, smoking; I, Suicide ideation; A, Suicide attempt; D, Suicide death.

Discussion

Main finding of this study

We summarized the available evidence from cohort, case–control and cross-sectional studies addressing the association between SUD and suicide outcomes. Our results suggested that SUD is associated with an increased risk of suicide outcomes. However, there was an evidence of considerable heterogeneity across the studies. Part of the observed heterogeneity can be explained by the quality of the studies, because conducting analyses by study quality resulted in a notable reduction in heterogeneity. However, to explore other sources of heterogeneity, we performed a meta-regression. Despite the observed heterogeneity, none of the predictors became statistically significant. That means the variables that we included in the meta-regression had a limited effect on the observed heterogeneity. In addition, the length of follow-up had no significant effect on the heterogeneity, because the results of cohort studies were reported separately. However, the observed heterogeneity is a multifactorial phenomenon that may be affected by several variables other than what were explored in the meta-regression such as difference in the sociocultural characteristics of the populations, the method of assessing exposure and outcome, and type, frequency, dose and way of substances used.

What is already known on this topic?

Suicide is a multifactorial phenomenon with several psychological, social, biological, cultural and environmental factors.[7,68,69] Psychiatric disorders, history of previously attempted suicide and[4] alcohol use disorder[9,10] are among the major risk factors for suicide. Several epidemiological studies have investigated the effect of illicit drugs on suicide outcomes, but the results are generally inconsistent. To date, a few meta-analyses[15,16] have been performed to estimate the overall association between substance abuse and suicide behaviors, but these meta-analyses were associated with some limitations and biases. The main limitation of these studies was that they did not explore the effect of SUD on different types of suicide outcomes.

Carrà *et al.*[16] conducted a meta-analysis of literature published before 2013 to assess the effect of co-occurring bipolar disorder, alcohol use disorder and SUD on suicide attempt. They found 29 eligible studies involving 31 294 participants. They reported ORs of 1.77 (95% CI: 1.49, 2.10) and 1.96 (95% CI: 1.56, 2.47) for SUD alone and combined SUD and alcohol disorder, respectively. They concluded that SUD, particularly if it is associated with alcohol use disorder, can increase the risk of attempted suicide.

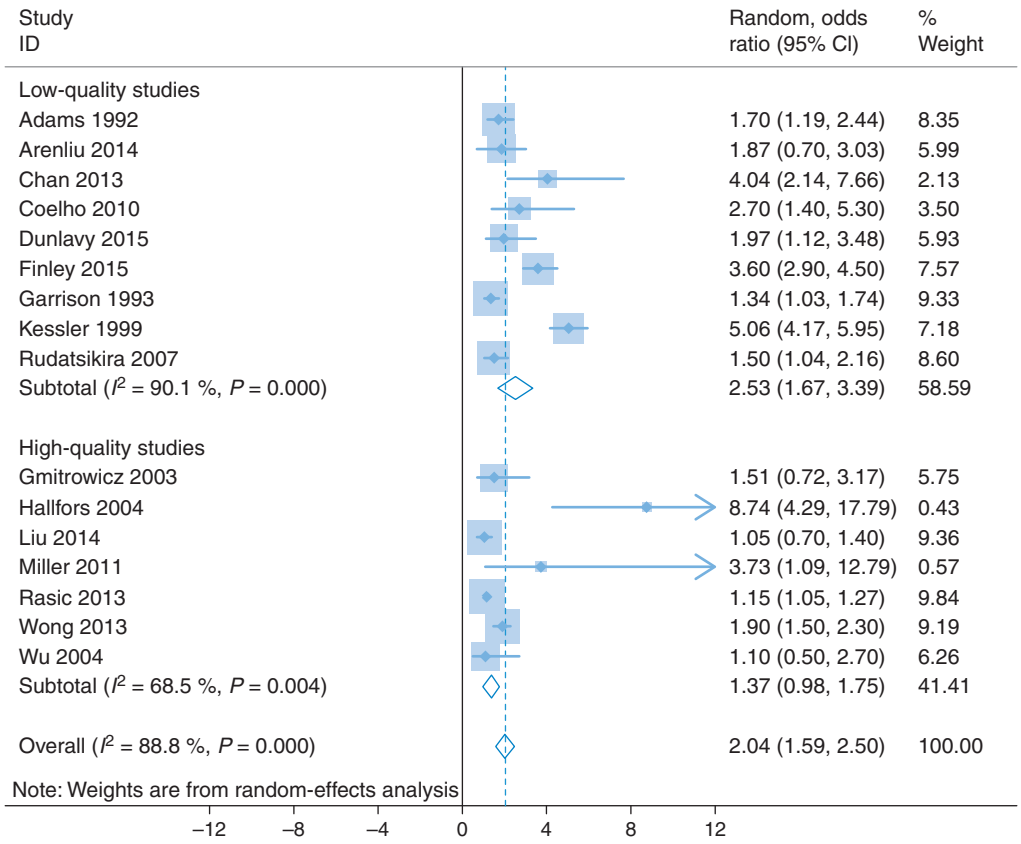

Fig. 2 Forest plot of the association between substance use disorder and suicide ideation.

An old empirical review of cohort studies was conducted by Wilcox *et al.*[15] on English language reports indexed in Medline before 2002 to explore the association between SUD and suicide death. They reported that standardized mortality ratios for suicide was 1351 (95% CI: 1047, 1715) among opioid users, 1373 (95% CI: 1029, 1796) among intravenous drug users and 1685 (95% CI: 1473, 1920) among mixed drug users. This review revealed that not only type of substance, but also the way they are used have an impact on suicide outcomes.

What this study adds?

This meta-analysis could efficiently estimate the association between SUD and suicide ideation, suicide attempt and suicide death, separately. In addition, a wide search strategy was developed and several databases were searched to increase the sensitivity of the search to include as many studies as possible. We assessed all types of observational studies irrespective of age, country, race, publication date and language. We screened 12 413 references and included 43 eligible studies in the meta-analysis involving 870 967 participants. Thus, the evidence was sufficient to make a conclusion regarding the objective of the study for estimating the association between SUD and suicide.

However, the evidence comes mainly from cross-sectional and case–control studies conducted in both developed and developing countries. However, the number of cohort studies addressing the association between SUD and suicide is limited. Therefore, we need further evidence based on long-term prospective cohort studies to make a robust conclusion about the risk of suicide caused by illicit drug use. Furthermore, there is insufficient evidence in regard to the effect of various types of substance on suicide and the dose–response relationship between SUD and suicide outcomes. Thus, further investigations based on observational studies are needed to expect the dose–response pattern of SUD-related suicide.

Limitations of this study

Our study had a few limitations as follows. First, the results were associated with a considerable heterogeneity. We performed a meta-regression to explore the sources of heterogeneity. However, no significant factor was found to explain the observed heterogeneity. Second, wherever possible, we

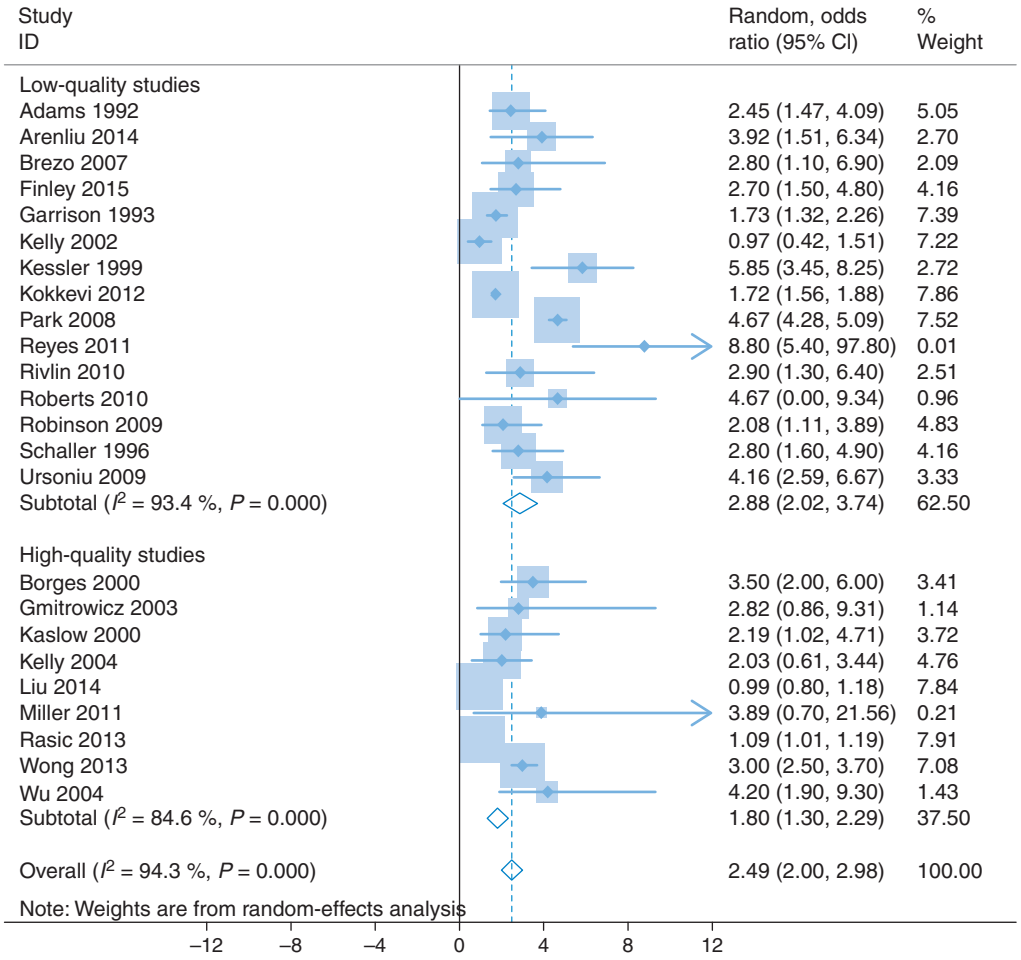

Fig. 3 Forest plot of the association between substance use disorder and suicide attempt.

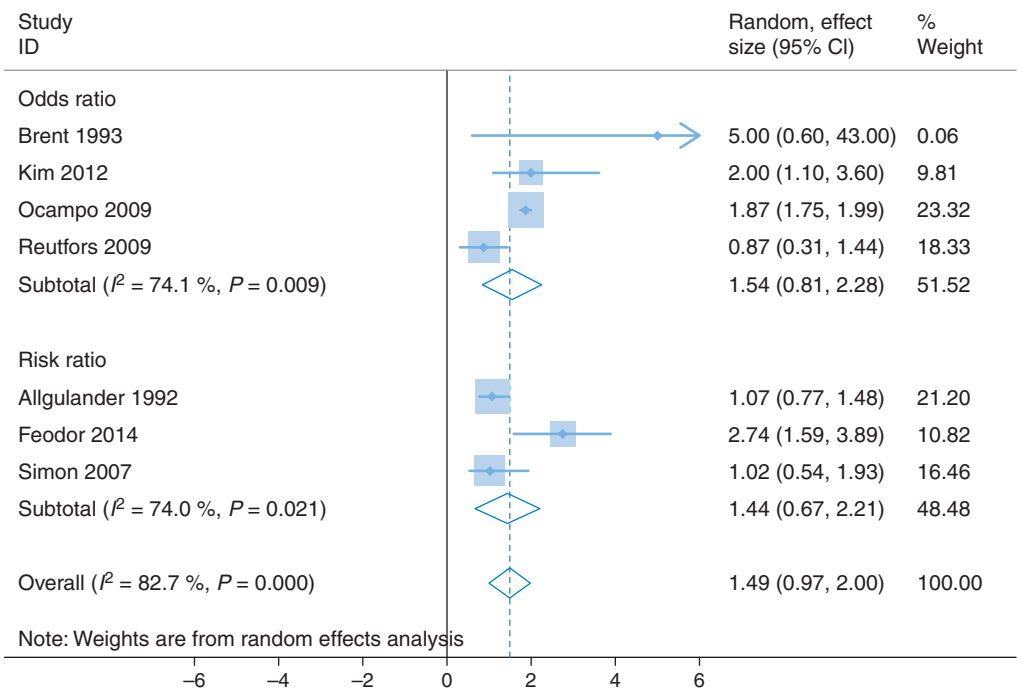

Fig. 4 Forest plot of the association between substance use disorder and suicide death.

Table 2 Results of subgroup analysis by suicide type (ideation, attempt and death) based on the types of substance and adjustment for different confounders

Variables	*Suicide ideation*				*Suicide attempt*				*Suicide death*			
	OR (95% CI)	*No.*	I^2	*Q-test*	*OR (95% CI)*	*No.*	I^2	*Q-test*	*OR (95% CI)*	*No.*	I^2	*Q-test*
Substance												
Cannabis	1.16 (0.70, 1.63)	2	66.9%	0.082	1.06 (0.77, 1.34)	7	76.8%	0.001	No data	0	No data	No data
Cocaine	1.27 (0.81, 1.72)	3	92.0%	0.001	1.79 (0.85, 2.74)	5	95.0%	0.001	No data	0	No data	No data
Marijuana	1.34 (0.96, 1.73)	3	86.8%	0.001	1.60 (1.45, 1.75)	3	00.0%	0.510	No data	0	No data	No data
Opioid	1.34 (0.29, 2.40)	2	95.1%	0.001	1.95 (0.05, 3.96)	2	97.6%	0.001	No data	0	No data	No data
Adjustment												
Unadjusted	2.00 (1.39, 2.61)	7	78.1%	0.001	2.95 (1.68, 4.21)	11	93.3%	0.001	1.87 (1.75, 1.98)	3	00.0%	0.939
Adjusted	2.45 (1.45, 3.46)	8	92.5%	0.001	2.29 (1.75, 2.83)	12	89.5%	0.001	3.98 (2.24, 10.21)	2	97.4%	0.001

Table 3 Results of meta-regression analysis assessing the effect of types of substance, adjustment for different confounders, sex ratio and mean age on the overall estimated effect size

Variables	*Coef.*	*Std. Err.*	t	P-*value*	*95% CI*
Suicide ideation					
Substance	−0.05	0.09	−0.63	0.535	−0.23, 0.13
Sex ratio	2.34	1.23	1.90	0.074	−0.25, 4.92
Mean age (years)	0.01	0.02	−0.02	0.982	−0.05, 0.05
Adjustment	0.26	0.25	1.05	0.308	−0.26, 0.79
Constant	−0.61	0.62	−0.98	0.341	−1.91, 0.70
Suicide attempt					
Substance	−0.06	0.08	−0.74	0.465	−0.23, 0.11
Sex ratio	0.37	0.59	0.63	0.535	−0.83, 1.56
Mean age (years)	0.01	0.02	0.39	0.703	−0.03, 0.04
Adjustment	−0.36	0.21	−1.73	0.094	−0.77, 0.06
Constant	0.74	0.49	1.50	0.144	−0.27, 1.76
Suicide death					
Substance	−0.82	0.85	−0.97	0.434	−4.47, 2.83
Sex ratio	0.04	0.02	1.80	0.213	−0.06, 0.14
Mean age (years)	−0.12	0.06	−2.12	0.168	−0.37, 0.13
Adjustment	0.21	0.72	0.30	0.796	−2.89, 3.31
Constant	5.20	1.91	2.73	0.112	−3.01, 13.42

Substance: 1, drugs; 2, cannabis; 3, marijuana; 4, opioid; Adjustment: 0, unadjusted; 1, adjusted; Sex ratio: male/female percentage.

used the full adjusted forms of OR controlling for confounding factors. However, the confounding effect was not completely ruled out, because some studies reported crude forms of OR estimates. This issue may lead to measurement bias. Finally, a definite cut point was not specified in the Newcastle Ottawa Statement Manual to differentiate high-quality studies from low-quality ones. Therefore, we had to define a cut point (seven star items or more for high-quality studies and six star items or less for low-quality studies) according to our own experience.[11,20,21] This cut point was determined logically, but not ideally. Therefore, this may raise the possibility of differential bias. Based on this categorization, the methodological quality of 23 out of 43 studies was low. Therefore, we presented the results of meta-analysis for high- and low-quality studies in separate.

Conclusion

This meta-analysis estimated the effect of SUD on suicide outcomes. Based on the current evidence, SUD is strongly associated with an increased risk of suicide ideation, suicide attempt and suicide death. Therefore, illicit drugs of any kinds can be considered important predictors of suicide and hence a great source of premature death.

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