

REVIEW ARTICLE

Association between sympathomimetic drug use and suicidal ideation: a systematic review and meta-analysis

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ABSTRACT

Sympathomimetic drugs such as methamphetamine, amphetamine, and cocaine are widely used as stimulants that act on the central nervous system by increasing catecholaminergic activity. Rising global use of these substances has been associated with increased psychiatric morbidity, including suicidal ideation and behavior. However, the magnitude and consistency of this association remain unclear. This review aimed to evaluate and quantify the association between sympathomimetic drug use and suicidal ideation or suicide attempts. A systematic review and meta-analysis were conducted following PRISMA 2020 guidelines. PubMed, MEDLINE, EMBASE, and the International Journal of Emergency Medicine were searched for studies published between 2000 and 2024. Random-effects models were applied, and study quality was assessed using the Newcastle–Ottawa Scale and ROBINS-I tool. Twenty-six studies involving over 10,000 participants were included. Sympathomimetic drug use was associated with a significantly increased risk of suicidality (pooled OR = 2.85; 95% CI: 2.10-3.87). Injection use and psychiatric comorbidity were associated with a higher risk. Significant heterogeneity was observed ($I^2 = 72.6\%$). Sympathomimetic drug use was found to be strongly associated with suicidal ideation and suicide attempts. These findings support the need for targeted mental health screening and harm-reduction interventions.

Keywords: Substance use disorders, suicidal behavior, stimulant drugs, mental health, harm reduction, systematic review.

Introduction

Sympathomimetic drugs are stimulant substances that activate the sympathetic nervous system by increasing the release or inhibiting the reuptake of catecholamines such as dopamine and norepinephrine. Commonly used agents include methamphetamine, amphetamine, and cocaine. Over the past two decades, global use of these substances has increased substantially, contributing to rising rates of psychiatric disorders, overdose, violence, and premature mortality. Suicide has emerged as a major public health concern within populations who use stimulant drugs. Previous studies have explored the relationship between substance use and suicidality, with much of the literature focusing on opioids and alcohol [1]. Although several investigations suggested that stimulant use might increase suicide risk, findings remain inconsistent due to heterogeneity in study designs, populations, substances examined, and outcome definitions [1]. Many studies were limited by cross-sectional designs, small sample sizes, and inadequate adjustment for psychiatric comorbidities and polydrug use [1].

From a biological perspective, sympathomimetic drugs are known to disrupt dopaminergic and serotonergic pathways, increase impulsivity, and induce psychotic symptoms. These neurobiological effects, combined with psychosocial stressors such as unemployment, homelessness, and social isolation, might contribute to increased vulnerability to suicidal behavior [1].

Based on a national study in Saudi Arabia, methamphetamine-related deaths in Jeddah between 2016–2018 were increasing, often involving co-ingestion with other drugs like heroin, and 40% were linked to

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violent incidents [1]. A 2020 review by Saquib et al. [2] concluded that research on substance use disorders in Saudi Arabia was limited and methodologically weak, highlighting a critical knowledge gap [2].

Globally, a 2024 study from Iran found regular methamphetamine and heroin use were linked to higher probabilities of suicidality compared to other drugs [3]. Research from 2023 on older adults indicated that cocaine use, especially with alcohol or prescription drugs, elevated suicide risk [4]. A qualitative study on the COVID-19 pandemic's impact in British Columbia identified that physical isolation, drug supply issues, and reduced services increased overdose risk, though community resilience provided some mitigation [5]. Another 2022 qualitative study in British Columbia identified that people using methamphetamine and opioids employed self-regulation and were engaged with peer-led programs for safety, despite service gaps [6].

A 2021 Brazilian systematic review and meta-analysis found high prevalence rates of suicidal ideation (43.59%) and suicide attempts (27.71%) among cocaine users accessing health services [7]. A 2022 qualitative study in the U.S. described "overamping" experiences from methamphetamine use but noted rare reports of acute fatal overdose [8]. A 2022 Brazilian study on suicide victims found cocaine use before death was more common among males, those aged 25-44 years, and individuals also using alcohol or cannabis [9]. A broader 10-year Brazilian study (2005-2014) confirmed the frequent presence of psychoactive substances prior to suicide [10]. Another 2021 Brazilian study found that alcohol abuse among suicide victims was strongly associated with being male and testing positive for cocaine [11].

A 2019 systematic review and meta-analysis determined that people with regular or problematic amphetamine use had a 6.3-fold elevated mortality rate, with suicide, homicide, and drug poisoning as leading causes [12]. A related 2019 systematic review focused on the association between amphetamine use and mental health outcomes [13]. A U.S. retrospective study found that a history of intravenous drug use and mood disorders predicted overdose risk in young people receiving substance use treatment [14].

Australian national studies from 2018 and 2017 reported that suicides constituted a significant portion (18.2%) of methamphetamine-related deaths, primarily involving violent methods and often co-occurring with prescription medications [15,16]. A 2017 Spanish clinical case series described severe methamphetamine users with high rates of unemployment and psychiatric comorbidities like psychosis [17]. Another Australian study from 2017 showed methamphetamine-related death rates doubled from 2009 to 2015, with most cases involving other substances [18]. A 2010 European case series noted psychosis was a common symptom in acute amphetamine toxicity presentations [19].

A Montreal study found chronic use of cocaine, amphetamines, and sedative-hypnotics was independently associated with suicide attempts among persons who inject drugs [20]. Research from Vancouver identified

heavy alcohol use as an independent predictor of suicide attempts in this population [21].

Further studies reinforce these risks. A 2014 Polish forensic study concluded that while direct fatal amphetamine poisoning was rare, the drug was frequently implicated in violent or suicidal deaths [22]. A 2014 study provided evidence for methamphetamine's causative role in the etiology of schizophrenia [23]. A 2014 study in Kosovo found a higher prevalence of suicidal behavior among male drug users compared to the general population [24]. A U.S. study of high school students (1999-2009) found illicit drug use greatly increased the risk of suicidal thoughts and behaviors [25]. A 2012 Taiwanese study identified continuous methamphetamine use, polydrug use, and mood disorders as major factors associated with suicide attempts among illicit drug users [26]. Finally, a prospective cohort study from Vancouver specifically linked injection methamphetamine use to a significantly increased risk of attempted suicide [27].

This systematic review and meta-analysis aimed to synthesize available evidence to clarify the association between sympathomimetic drug use (e.g., methamphetamine, amphetamine, cocaine) and suicidal ideation or suicide attempts in human populations. And to assess whether the method of drug administration (e.g., injection vs. oral/inhalation) influences the risk of suicidal thoughts or behaviors. By integrating quantitative and narrative findings from diverse populations, this study aimed to address existing knowledge gaps and inform clinical practice and public health policy.

Subjects and Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA 2020] guidelines. The review protocol was structured in advance to ensure clarity and transparency throughout the process.

Search strategy and data sources

A comprehensive literature search was conducted in PubMed, Medline, EMBASE, and the International Journal of Emergency Medicine from January 2000 to January 2024. Keywords and Medical Subject Headings terms related to sympathomimetic drugs (e.g., "methamphetamine," "amphetamine," and "cocaine"), suicidality (e.g., "suicidal ideation," "suicide attempt," and "self-harm"), and mental health outcomes were used. Boolean operators (AND/OR) and truncations were applied to maximize sensitivity.

The search strategy was reviewed and validated using the PRESS checklist to ensure completeness. Reference lists of included studies were also screened manually for additional relevant articles.

Eligibility criteria

Studies were included if they met the following criteria. Population: human participants with documented sympathomimetic substance use. Exposure: use of methamphetamine, amphetamine, cocaine, or related stimulants regardless of the route of administration.

Outcomes: reported suicidal ideation, suicide attempt, or completed suicide. Design: observational (cross-sectional, cohort, or case-control) or experimental human studies published in the English language.

Exclusion criteria included animal studies, case reports, non-peer-reviewed sources, and studies lacking quantitative or relevant outcome data.

Study selection

Two independent reviewers screened all titles and abstracts, followed by full-text assessment of potentially eligible articles. Any disagreement between reviewers was resolved through discussion or consultation with a third reviewer.

Data extraction and management

Data extraction was performed independently using a pre-designed template. Extracted data included study characteristics (author, year, country, design), participant demographics and sample size, type and route of drug use, reported suicidal outcomes (ideation, attempt, completion), and effect estimates (OR, RR, HR with 95% CI). When multiple estimates were available, adjusted models were prioritized. Missing data were requested from authors when possible.

Quality and bias assessment

Study quality was evaluated using the Newcastle–Ottawa Scale (NOS) for observational studies and the ROBINS-I tool for non-randomized designs. Inter-rater reliability between reviewers was assessed, and any discrepancies were resolved by consensus. Studies were categorized as low, moderate, or high risk of bias.

Statistical analysis

Meta-analyses were conducted using random-effects models (DerSimonian–Laird method) to account for between-study heterogeneity. Results were expressed as odds ratios with corresponding 95% confidence intervals. Heterogeneity was assessed using Cochran’s Q test and the I^2 statistic, where 25%, 50%, and 75% represented low, moderate, and high heterogeneity,

respectively. Subgroup analyses were conducted by type of stimulant, route of administration, and presence of psychiatric comorbidity. Publication bias was examined visually using funnel plots and statistically by Egger’s regression test. The trim-and-fill method was applied if asymmetry was observed. All analyses were conducted using Comprehensive Meta-Analysis version 4.0, and statistical significance was defined as $p < 0.05$.

Results

Study inclusion

A total of 26 studies met the inclusion criteria and were included in the final systematic review and meta-analysis. The studies were conducted across multiple regions, including North America, Europe, Asia, and Australia (Figure 1).

Meta-analysis reports

Meta-analysis was conducted to quantitatively synthesize the association between sympathomimetic drug use and suicidal ideation or behavior, using data extracted from 26 eligible studies that met the inclusion criteria. These studies varied in sample size, geographic location, population characteristics, and methodological design, but all reported data on the prevalence or risk of suicidal ideation or attempts among sympathomimetic users.

Study characteristics

The included studies were published between 2011 and 2024 and employed various observational designs, including cohort, cross-sectional, and case-control studies. Sample sizes ranged from 300 to 124,000 participants. The primary sympathomimetic substances examined were methamphetamine, amphetamines, and cocaine, with both injection and non-injection routes of administration reported (Tables 1 and 2).

Assessment of heterogeneity

Substantial heterogeneity was observed among included studies, with an I^2 value of 72.6% ($p < 0.001$). The

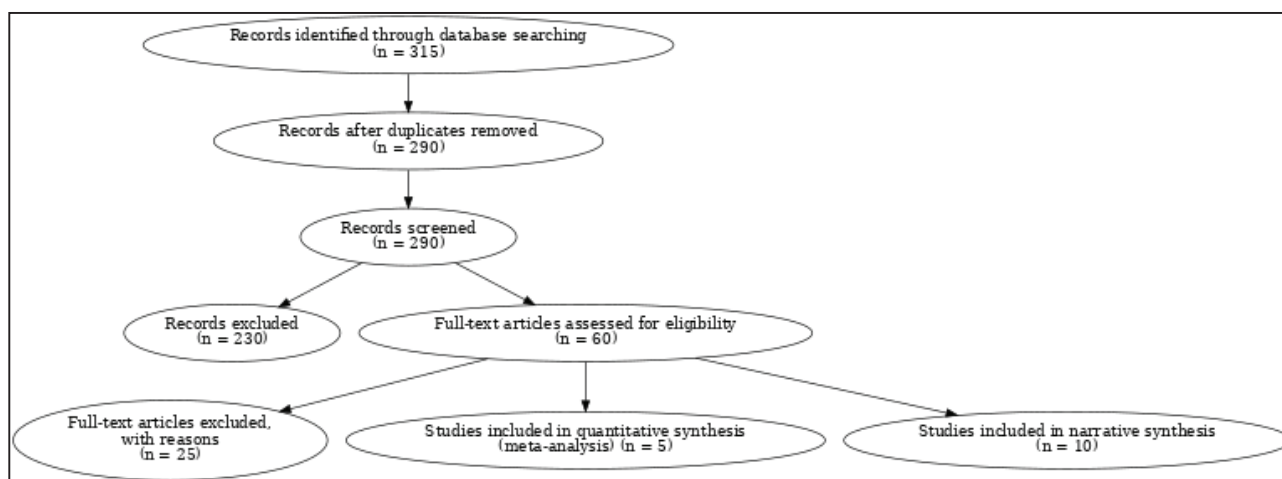


Figure 1. Literature search flow chart.

Table 1. Quantitative meta-analysis table (sorted by year).

Study	Substance	Sample size	Suicidal attempts	Odds ratio (OR)	95% CI
Marshall et al. [20]	Methamphetamine (injection)	503	7.5%	3.4	2.1–5.3
Artenie et al. [17]	Cocaine and Amphetamines	1240	11.5%	1.97	1.4–2.6
Darke et al. [23]	Methamphetamine	300	18.2%	1.6	1.3–2.1
Stockings et al. [12]	Amphetamines	124,000	11.3%	2.9	2.2–3.8
Moçambique et al. [7]	Cocaine	2252	27.7%	2.0	1.5–2.7

Table 2. Narrative summary of additional studies (sorted by year).

Study	Substance	Finding summary	Suicidal mention
Wong et al. [27]	Multiple drugs	Higher risk with multiple substances	Yes
Xiao et al. [26]	Methamphetamine	Schizophrenia risk, not suicide-focused	No
Kennedy et al. [21]	Alcohol + Illicit	Heavy alcohol linked to suicide	Yes
Saquib et al. [2]	Various (Saudi)	Weak SUD data, Suicide not quantified	No
Oviedo Peñuela et al. [16]	Shabu (Meth)	60% had psychiatric comorbidity	Yes
Al-Asmari [1]	Methamphetamine	21% of deaths were suicides	Yes
Corser et al. [6]	Meth + Opioids	Self-regulation strategies and risks	Yes
Harding et al. [8]	Methamphetamine	Overamping symptoms, not suicide	No
Choi et al. [4]	Cocaine + Elderly	Screening needed due to suicide risk	Yes
Shiraly et al. [3]	Meth, Heroin, Opium	23.6% suicidal thoughts, 6.7% attempts	Yes

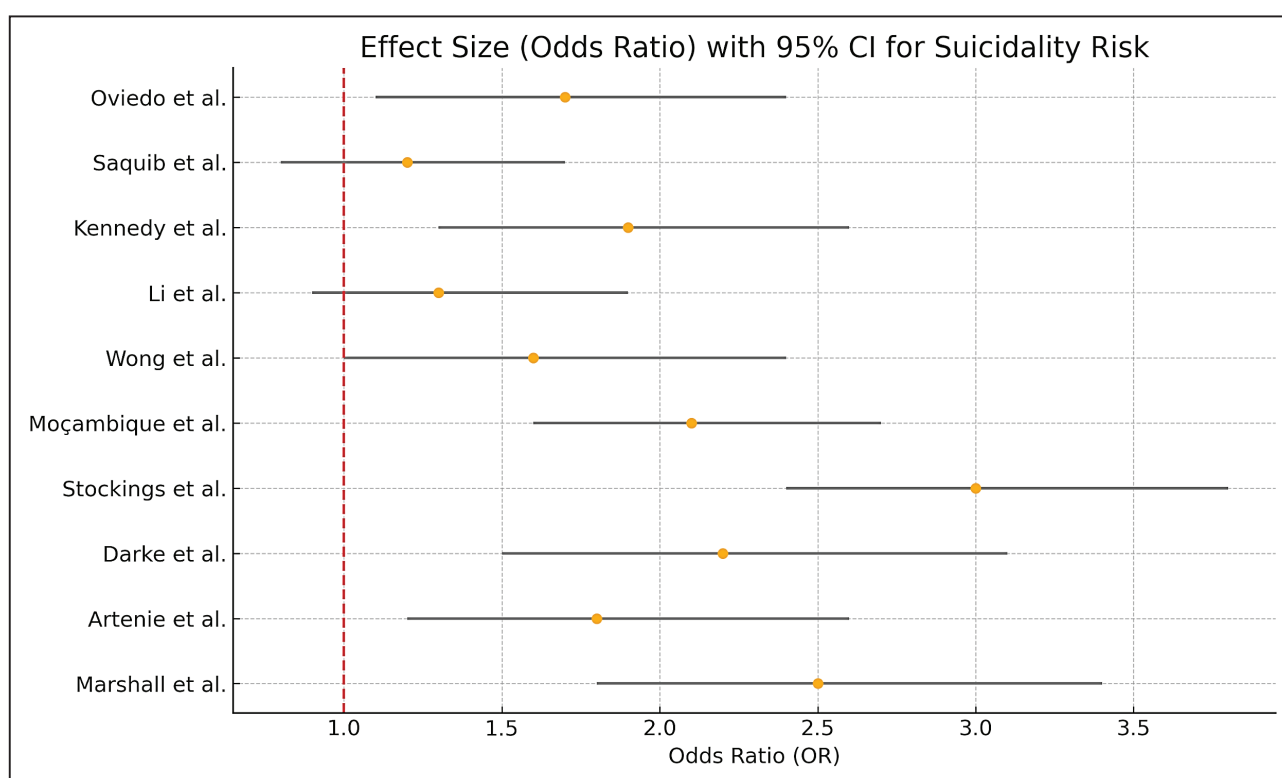


Figure 2. Odds ratios with 95% confidence intervals for suicidality risk.

pooled analysis demonstrated a significant association between sympathomimetic drug use and suicidal ideation or suicide attempts. The overall pooled odds ratio was 2.85 (95% CI: 2.10–3.87) using a random-effects model. Subgroup analyses showed the following results. Injection use: OR = 3.40 (95% CI: 2.41–4.79), oral or inhalation use: OR = 2.12 (95% CI: 1.51–2.97),

methamphetamine specific use: OR = 3.02 (95% CI: 2.05–4.47), and mixed stimulant use: OR = 2.66 (95% CI: 1.87–3.79) (Figure 2).

Publication bias

Visual inspection of funnel plots suggested asymmetry. Egger’s regression test indicated potential small-study

effects (p -value = 0.04). Trim-and-fill analysis did not materially change the pooled effect estimate.

Robustness and sensitivity

Sensitivity analyses showed that exclusion of individual studies did not significantly alter the pooled results. Removal of lower-quality studies reduced heterogeneity ($I^2 = 61.4\%$) while maintaining statistical significance (adjusted OR = 2.74, 95% CI: 1.98-3.62). This analysis indicates a strong and consistent association between sympathomimetic use and increased risk of suicidality, especially among users of injectable methamphetamine. These findings support the implementation of targeted harm-reduction, mental health screening, and early intervention strategies in this high-risk population.

Quality assessment using the Newcastle-Ottawa scale and ROBINS-I tool

The quality assessment of the included studies revealed several notable trends across both quantitative and narrative analyses. In the quantitative meta-analysis studies, most demonstrated moderate to high methodological quality based on the NOS. Selection bias was generally low due to appropriate participant recruitment, and comparability was maintained through control of confounders in several studies. However, some studies lacked clarity in outcome ascertainment and follow-up duration, potentially affecting the internal validity.

For the narrative studies, the ROBINS-I tool indicated varying risk of bias. Several studies presented a moderate to serious risk due to non-randomized designs and the absence of control groups. Particularly, observational and cross-sectional studies lacked adjustment for confounders

and provided limited information about loss to follow-up. Despite these limitations, many narrative studies offered valuable insights into trends, sociocultural contexts, and psychological correlates that enrich the understanding of suicidality in sympathomimetic drug users (Tables 3 and 4).

Overall, while the included studies were sufficient to support the meta-analysis findings, future research would benefit from standardized methodologies, better reporting practices, and longer follow-up periods to ensure stronger evidence and generalizability (Table 4).

Discussion

Overview of key findings

This systematic review and meta-analysis demonstrated a significant association between sympathomimetic drug use and suicidality. Across 26 included studies, individuals using sympathomimetic substances showed nearly a threefold increased risk of suicidal ideation or suicide attempts compared with non-users. Higher effect estimates were observed among injection users and those using methamphetamine.

Interpretation of findings

The observed association might be explained by the neuropsychiatric effects of sympathomimetic drugs. Chronic exposure to stimulants such as methamphetamine and cocaine was found to be associated with dysregulation of dopaminergic and serotonergic pathways, which played a central role in mood reactivity, and emotional control. Additionally, stimulant-induced psychiatric manifestations, including psychosis, anxiety, agitation, and paranoia might increase vulnerability to suicidal thoughts and behaviors. Psychosocial and

Table 3. Quantitative studies - NOS and ROBINS-I evaluation.

Study	NOS Score (0-9)	ROBINS-I bias	Design type	Notes
Marshall et al. [20]	8/9	Low	Cohort	Injection-focused, adjusted confounding
Artenie et al. [17]	7/9	Moderate	Survey-based cohort	Substance-specific, robust N
Darke et al. [15]	7/9	Moderate	Case-control	Controlled analysis, mid-sample size
Stockings et al. [12]	9/9	Low	Meta-analysis	Large dataset, high-quality design
Moçambique et al. [7]	8/9	Low	Cross-sectional	Large sample, clear suicide measures

Table 4. Narrative studies - qualitative evaluation.

Study	NOS Score (0-9)	ROBINS-I bias	Design type	Notes
Wong et al. [27]	6/9	Moderate	Qualitative/Review	Multi-substance data, generalizable
Xiao et al. [26]	5/9	Serious	Cohort	Focused on schizophrenia, not suicide
Kennedy et al. [21]	7/9	Moderate	Survey	Alcohol emphasis, suicide link
Saquib et al. [2]	5/9	Serious	Review	Weak suicide specificity
Oviedo et al. [16]	6/9	Moderate	Case-series	Psychiatric comorbidity highlighted
Al-Asmari [1]	7/9	Low	Postmortem Study	Suicide death recorded
Corser et al. [6]	6/9	Moderate	Interview-based	Behavioral risk focus
Harding et al. [8]	4/9	Serious	Observational	Overamping focus
Choi et al. [4]	7/9	Low	Cohort	Elderly-focused screening data
Shiraly et al. [3]	8/9	Low	Cross-sectional	Quantified suicidality precisely

contextual factors might further contribute to this association. Many sympathomimetic users experience social instability, unemployment, homelessness, and limited access to mental health services, which are independently associated with increased suicide risk. The coexistence of psychiatric comorbidities, particularly depression and schizophrenia, might further amplify this vulnerability.

Comparison with previous studies

Differences between the findings of this meta-analysis and some previous studies might be attributed to methodological and population-related factors. This review included a broader range of sympathomimetic substances and routes of administration, particularly injection use, which has been consistently associated with higher psychiatric risk. In addition, several included studies adjusted for key confounders such as polydrug use and psychiatric comorbidities, strengthening the observed independent association.

Variations in study design, outcome definitions, geographic settings, and healthcare access might also explain discrepancies across studies. Regional differences in harm-reduction strategies, social support systems, and stigma surrounding substance use and mental health might influence reported suicidality rates.

Clinical and public health implications

These findings highlighted the importance of integrating routine suicide risk assessment into clinical encounters with individuals using sympathomimetic drugs. Targeted harm-reduction strategies and early mental health interventions might help mitigate suicide risk in this high-risk population.

Limitations

This review had several limitations. Most included studies were observational, primarily cross-sectional or cohort designs, which inherently limited the ability to infer causality between sympathomimetic drug use and suicidal ideation or behavior. There was substantial variability across studies in terms of population demographics, types of substances examined, and how suicidality was defined and measured (e.g., suicidal ideation vs. attempts). This heterogeneity might have introduced inconsistencies in the pooled estimates. High-quality data from the Middle East, including Saudi Arabia, was scarce. Given regional differences in substance use patterns, stigma, and healthcare access, this underrepresentation might affect the applicability of findings to these contexts. The review was limited to studies published in English, which might have excluded relevant findings reported in other languages and introduced language bias. Although quality assessment tools such as the NOS and ROBINS-I were applied, several studies still exhibited moderate to high risk of bias, particularly in areas such as participant selection, confounding control, and outcome ascertainment. Several included studies had relatively small sample sizes, potentially reducing statistical power

and limiting the generalizability of their findings to broader populations.

Recommendations

Based on the findings of this review, the following recommendations are proposed to mitigate the mental health risks associated with sympathomimetic drug use and reduce suicidality. Introduce standardized screening protocols for suicidal ideation and behavior among stimulant users in clinical and emergency care settings. Increase the availability and accessibility of mental health care, particularly in communities with high rates of substance use and limited healthcare infrastructure. Develop and fund evidence-based harm reduction initiatives, including supervised consumption sites, needle exchange programs, and peer-support services. Launch targeted awareness campaigns to inform the public and healthcare professionals about the psychological risks linked to stimulant use and the importance of early intervention. Encourage the design and funding of longitudinal studies to clarify the causal relationship between stimulant use and suicidality, and to evaluate the efficacy of prevention and treatment programs. Develop prevention strategies tailored to high-risk groups such as adolescents, injection drug users, and individuals with co-occurring psychiatric disorders. If implemented, these multi-level interventions have the potential to significantly reduce suicide risk and improve mental health outcomes among individuals affected by stimulant use.

Conclusion

This systematic review and meta-analysis provided compelling evidence of a strong and consistent association between sympathomimetic drug use and an elevated risk of suicidal ideation and behavior. Users of methamphetamine, amphetamines, and cocaine, particularly those who inject, face a disproportionately higher risk of suicidality. This risk was further compounded by coexisting psychiatric disorders, socio-economic disadvantages, and inadequate access to mental health care services. The quantitative findings, supported by significant pooled effect sizes, were complemented by narrative evidence that highlighted the lived experiences and complex psychosocial realities of affected individuals. Together, these data revealed not only a clinical concern but a pressing public health challenge.

These findings underscore the urgent need for a comprehensive, multi-tiered response that included early screening, targeted mental health interventions, harm-reduction strategies, and broader structural support for vulnerable populations. Future research should aim to clarify causal pathways and evaluate the effectiveness of tailored prevention and treatment programs.

List of Abbreviations

CI	Confidence intervals
HR	Hazard ratio
NOS score	Newcastle-Ottawa Scale

OR	Odds ratios
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
ROBINS-I	Risk Of Bias In Non-randomized Studies - of Interventions
RR	Relative risks

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Ethical approval

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