

REVIEW ARTICLE

Prevalence of suicide in cocaine users accessing health services: a systematic review and meta-analysis

Milton Moçambique,^{1,2} Aline Hoffmann,¹ Vinícius S. Roglio,^{1,2} Felix H.P. Kessler,^{1,2} Carla Dalbosco,¹ Jaqueline B. Schuch,^{1,2} Flavio Pechansky^{1,2}

¹Centro de Pesquisas em Álcool e Drogas, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. ²Programa de Pós-Graduação em Psiquiatria e Ciências do Comportamento, UFRGS, Porto Alegre, RS, Brazil.

Objective: This study reviewed and analyzed the prevalence of suicidal behaviors among cocaine users who sought health services.

Methods: This is a systematic review and meta-analysis of studies published until January 2021. PubMed/MEDLINE, Scopus, Embase, PsycINFO, and LILACS were searched. The inclusion criteria were observational (retrospective or prospective), case-control, and/or cross-sectional reports that contained samples of cocaine users aged over 14 years who were assessed in health facilities or were in treatment. The random-effects model was used to calculate the overall prevalence of suicidal behavior with a 95% confidence interval. Subgroup analysis was conducted to investigate sources of heterogeneity.

Results: Twenty articles were included, yielding a total of 2,252 cocaine users. The estimated prevalence was 43.59% (95%CI 31.10-57.38) for suicidal ideation and 27.71% (95%CI 21.63-34.73) for suicide attempts. High heterogeneity was found between studies for both outcomes ($I^2 \geq 93\%$), although subgroup analysis considering the quality of the studies showed a significant difference in suicide attempts ($p = 0.03$).

Conclusion: Cocaine use can be considered a risk factor for suicidal behavior, and prevention and early screening measures should be implemented to facilitate adequate treatment.

Keywords: Suicide; cocaine; addiction; substance use disorder

Introduction

Each year, about 800,000 people worldwide die from suicide, which is equivalent to one death every 40 seconds. Evidence suggests that for each adult who dies of suicide, more than 20 others may have attempted it.¹ The annual global suicide rate is estimated at 10.5 per 100,000 population,² accounting for 1.4% of all deaths worldwide, which makes it the 18th leading cause of death. The prevalence of suicidal ideation, plans, and attempts has been estimated at 2% by the World Health Organization for both developed and developing countries.³ This serious public health problem is related to other behaviors and clinical conditions and affects individuals of all ages. Evidence suggests that public health policies and low-cost interventions can help prevent suicide.⁴

The phenomenon of suicide comprises a series of behaviors: suicidal thinking (or ideation), suicide attempt (SA), and suicide itself.² Suicidal ideation (SI) involves a broad range of thoughts: a desire to die or the idea of self-destruction, with or without a plan of action.⁵ A SA is a potentially harmful behavior with a non-fatal outcome

accompanied by evidence that: the person intended to kill himself but failed and was rescued, the attempt was thwarted, or the person changed his mind.⁶ Suicide, on the other hand, refers to the act of deliberately killing oneself or fatal suicidal behavior. This complex phenomenon is associated with several risk factors, such as biological, psychological, social, environmental, and cultural aspects.¹ Other risk factors include previous SAs⁷ and their association with the use of alcohol and other drugs. Although several theories have been developed to explain suicidal behavior, the stress-diathesis model is the most comprehensive; it explains suicidal thoughts as the interaction between acquired vulnerabilities (conditioned and/or learned) and triggering stressors.⁸ These include genetic factors, trauma, a history of abuse or neglect, personality traits, psychiatric disorders, socioeconomic problems, discrimination, emotional imbalance, rejection, feelings of failure or helplessness, and chronic pain, etc.; the same factors are also associated with substance abuse and dependence.

Substance use disorder is among the main risk factors for suicide.^{9,10} The type of drug consumed, the amount

Correspondence: Milton Moçambique, Universidade Federal do Rio Grande do Sul, Rua Ramiro Barcelos, 2400, CEP 90040-060, Porto Alegre, RS, Brazil.

E-mail: miltonmocambique84@gmail.com

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used, and the degree of consumption are also contributing factors to suicide-related outcomes. SI seems to be relatively higher among cocaine users. Studies indicate that the prevalence of cocaine use in the days prior to suicide is around 9 to 20%.¹¹⁻¹³ Indeed, predicting SAs can be complex and challenging. An extensive meta-analysis of 365 studies found that models explaining suicide have become stagnant.⁹ However, it is clear that drug misuse is a critical element in exacerbated suicide risk – as well as a modifiable factor.

Studies in Brazil indicate that suicidal behaviors are frequent among crack users.^{14,15} Worldwide, there is still a lack of more robust analysis that combines results from different studies on suicidal behavior, especially among users of cocaine and its derivatives.⁴ The information must be gathered, organized, and analyzed, considering the essential aspects of suicide in this population. Thus, through a systematic review and meta-analysis, this study aimed to estimate the prevalence of SI and SA among users of cocaine and its derivatives who seek health services.

Methods

This systematic review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)¹⁶ and the Cochrane Handbook¹⁷; it was approved in the PROSPERO platform (no. CRD42020142057).

The research strategy included MeSH terms, in addition to the conventional terms: (suicide[mh] OR suicid*[tw]) AND (Cocaine[mh] OR Cocaine[tw] OR Cocaine-Related Disorders[mh] OR Cocaine Smoking[mh] OR Crack Smoking[tw]). The search covered articles published in the PubMed/MEDLINE, Scopus, Embase, PsycINFO, and LILACS electronic databases, including searching in other literature sources (the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior Catálogo de Teses e Dissertações, the Sucupira Platform, and Google Scholar).

The search was performed on January 10, 2021, and studies published up to this date were included in the systematic review. The initial selection of articles was based on title and abstract reading by two authors (MM and AH) separately. A third author (CD) was consulted when there was a need to evaluate conflicting articles.

Eligibility criteria

The inclusion criteria were observational (retrospective or prospective), case-control, and/or cross-sectional reports that contained samples of cocaine users aged over 14 years who were assessed in health facilities or were in treatment. There were no restrictions on sex, education level, language, or year of publication. We excluded community and household studies, or those with indigenous or prison populations who did not have access to health services. Studies with insufficient or overlapping data, or those that did not discriminate the outcome (SI or SA), qualitative studies, conference abstracts, and review articles (systematic or not, with or without meta-analysis)

were excluded. Articles in which the sample used cocaine in addition to other drugs were also excluded, since there was a chance of a confounding bias in the outcomes.

Data extraction and quality assessment of the studies

After article selection, two authors (MM and AH) extracted the data independently. The full texts of the eligible studies were reviewed, and the following data were extracted when possible: authors, year of publication, the sample's country of origin, age, sex, and characteristics (treatment regimen, multicenter study or not, study period, treatment-seeking), and the outcome (no suicidality, SI, and SA).

The quality of the included studies and the risk of bias were assessed using the Newcastle-Ottawa Statement.¹⁸ This scale provides a checklist of items to verify the risk of bias in included studies, scoring a maximum of nine points for the following domains: selection, comparability, exposure, and outcome. In this review, studies with seven points or more were considered high quality, while the others were considered low quality.

Statistical analysis

The synthesis of the studies included in this meta-analysis was structured according to SI and SA prevalence among cocaine users seen in health services, which are presented as forest plots. Variance estimation for the random-effects model was performed using the inverse method; logit transformation was used to analyze group prevalence data and estimate 95% confidence intervals (95%CI). Heterogeneity was assessed with the chi-square test,¹⁹ the I-square (I²) test, and the Higgins test,²⁰ using the restricted maximum likelihood method to estimate variance. Subgroup analyses were conducted to investigate sources of heterogeneity, including a meta-regression approach with the proportion of men and the mean age. Publication bias was investigated using Egger's regression test and a funnel plot analysis. All analyses were conducted in R version 3.6.1 and the meta 4.9-72 and metafor 2.1-0 packages.²¹

Results

Study selection

The electronic database search yielded 3,476 articles according to the above-described inclusion criteria. Rayyan²² software was used as a reference manager. First, all duplicate articles were removed (n=1,793). The remaining studies were evaluated for design, population, and the outcomes of interest. After reading the title and abstract, another 1,543 articles were excluded for not meeting the outcome or inclusion criteria.

The remaining 140 articles were independently read in full by two authors (MM and AH). At this stage, a third reviewer (CD) was requested to review eight controversial articles. Subsequently, 120 articles were excluded from the meta-analysis for the following reasons: 62 did not present the expected outcome; four were duplicates;

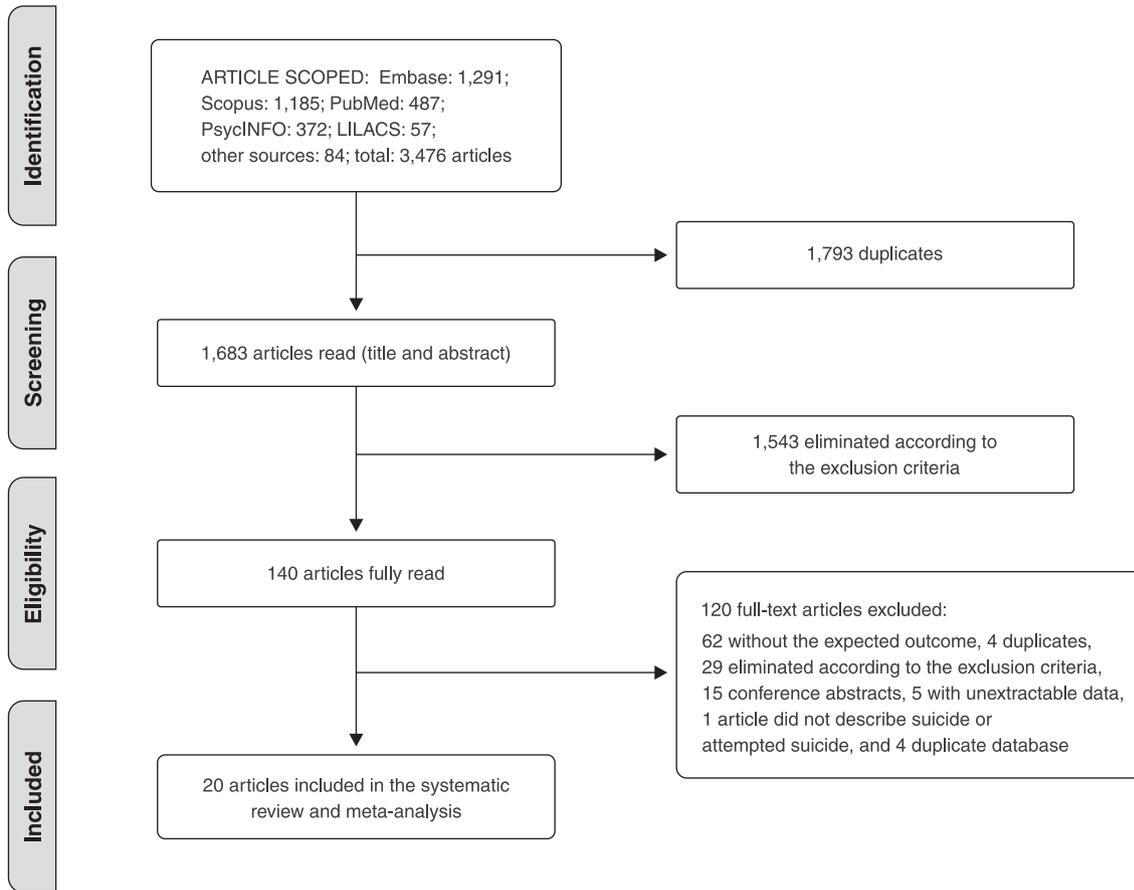


Figure 1 Article selection flowchart.

29 did not fulfil all the inclusion criteria (design, population, age); 15 were conference abstracts; one did not discriminate between SI and SA; and four involved the same (or part of the same) sample as previously included studies. In five studies, the data necessary for analysis could not be extracted; the authors of these studies were contacted by e-mail, but none replied. Thus, only 20 articles met the pre-established inclusion criteria and were included in the systematic review. Figure 1 is a flowchart of the article inclusion process.

Characteristics of the included studies

All 20 studies were cross-sectional.²³⁻⁴² Twelve were conducted in the United States,^{23-28,30,31,33,37,38,42} four in Brazil,^{32,35,39,41} two in Spain,^{36,40} one in Argentina,³⁴ and one in Chile.²⁹ The age of the participants ranged from 14 to 65 years. Most studies included both men and women and did not distinguish between SI and SA in the risk analysis. Some samples also included individuals in different categories of care (inpatient, outpatient, or both). The characteristics of these studies are summarized in Table 1.

Quality evaluation

The quality of the studies was assessed using the Newcastle-Ottawa Statement with some modifications. Fifteen

studies were good quality and the other five were low quality (Table 1).

Prevalence of suicidal ideation among users of cocaine and its derivatives (meta-analysis)

A meta-analysis based on ten studies was conducted to assess the SI outcome, finding a combined SI prevalence of 43.59% (95%CI 30.61-57.51) (Figure 2). This result showed high heterogeneity ($I^2 = 95\%$; $Q = 186.72$; $df = 9$, $p < 0.01$).

Prevalence of suicide attempts in users of cocaine and its derivatives (meta-analysis)

A separate meta-analysis of 12 studies was conducted to assess the SA outcome. The combined SA prevalence was 27.71% (95%CI 21.63-34.73) (Figure 3). There was also high heterogeneity among the studies for this result ($I^2 = 93\%$; $Q = 152.231$; degrees of freedom [df] = 11, $p < 0.01$).

Subgroup analysis

Due to the critical heterogeneity among the studies regarding the SI and SA outcomes, subgroup analyses were performed to identify possible sources of heterogeneity.

Table 1 Characteristics of the included studies

| Author | Country | Mean age (years) | Sex | Characteristics of the sample/diagnosis | Total users | NS | SI | SA | NOS |
|--------------------------|---------------|------------------|--------|--|-------------|-------|-----|-----|-----|
| Lowenstein ²³ | United States | 27.0 | Both | Outpatient and inpatient, not multicentric, diagnostic criteria not described | 115 | 97 | 18 | - | 5 |
| Rich ²⁴ | United States | 29.0 | Both | Outpatient, not multicentric, diagnostic criteria not described | 123 | 99 | - | 24 | 7 |
| Salloum ²⁵ | United States | 33.0 | Both | Outpatient, not multicentric, DSM-III | 25 | 3 | 22 | - | 6 |
| Dhossche ²⁶ | United States | 33.9 | Both | Outpatient, not multicentric, diagnostic criteria not described | 112 | 86 | - | 26 | 6 |
| Roy ²⁷ | United States | 41.4 | Both | Veteran outpatient, not multicentric, DSM-IV | 214 | 130 | - | 84 | 7 |
| Garlow ²⁸ | United States | 39.3 | Both | Outpatient, not multicentric, DSM-IV | 548 | 326 | 222 | - | 8 |
| Pérez ²⁹ | Chile | N/A | Both | Outpatient, not multicentric, diagnostic criteria not described | 61 | 28 | 30 | 14 | 3 |
| Cottler ³⁰ | United States | 32.2 | Both | Inpatient and outpatient, multicentric, diagnostic criteria not described | 685 | 319 | 367 | - | 7 |
| Ilgen ³¹ | United States | 32.8 | Both | Outpatient and inpatient, not multicentric, diagnostic criteria not described | 2,492 | - | - | 692 | 7 |
| Copersino ⁴² | United States | 31.0 | Female | Inpatient, not multicentric, DSM-IV-TR | 48 | 21 | 27 | - | 8 |
| Zubaran ³² | Brazil | 22.8 | Both | Inpatient, not multicentric, diagnostic criteria not described | 50 | 26 | - | 24 | 8 |
| Bohner ³³ | United States | N/A | Both | Inpatient and outpatient, multicentric, diagnostic criteria not described | 3,663 | 2,738 | - | 925 | 7 |
| Serfat ³⁴ | Argentina | N/A | Both | Treatment-seeking, outpatient, not-multicentric, diagnostic criteria not described | 68 | 52 | 16 | - | 8 |
| de Souza ³⁵ | Brazil | 27.9 | Both | Inpatient, not multicentric, Addiction Severity Index | 200 | - | 50 | 24 | 3 |
| Masferrer ³⁶ | Spain | 45.5 | Both | Inpatient, not multicentric, DSM-IV-TR | 25 | 8 | - | 17 | 8 |
| Walter ³⁷ | United States | 42.5 | Male | Inpatient, not multicentric, DSM-IV | 129 | 80 | - | 49 | 8 |
| Arias ³⁸ | United States | 36.0 | Both | Outpatient, not multicentric, diagnostic criteria not described | 72 | 50 | - | 22 | 7 |
| Silva ³⁹ | Brazil | 29.8 | Both | Inpatient, multicentric, DSM-IV-TR | 160 | 111 | - | 49 | 8 |
| Gofñi ⁴⁰ | Spain | 37.3 | Both | Treatment seeking, inpatient and outpatient, DSM-IV-TR | 163 | 100 | 63 | - | 8 |
| Roglio ⁴¹ | Brazil | 32.9 | Both | Inpatient, not multicentric, DSM-IV | 669 | - | 428 | 297 | 7 |

Data presented as n.

N/A = not available; NOS = Newcastle-Ottawa Statement; NS = no suicidality; SA = suicide attempt; SI = suicidal ideation.

The analyses were based on the following variables extracted from the articles: categories of care/treatment (inpatient, outpatient, or both), study quality (high or low), and whether it was a multicenter study (yes or no) (Table 2). For the SI outcome, these analyses showed no significant results, indicating that none of the factors influenced the results. However, there was a significant difference in study quality regarding SAs: high quality studies reported a higher SA prevalence ($p = 0.03$). Other subgroup analyses showed no significant differences.

Meta-regression analyses were conducted for age and sex. For sex, the proportion of men was not significantly associated with the prevalence of SI ($R^2 = 20.15\%$, $p = 0.158$, $n=6$) or SA ($R^2 = 0\%$, $p = 0.419$, $n=4$). Similar results were obtained for mean age (suicidal ideation presented $R^2 = 0\%$, $p = 0.292$, $n=9$; and SA presented $R^2 = 0\%$, $p = 0.703$, $n=10$).

Publication bias

Egger's regression test and funnel plot analysis revealed no potential publication bias for SI ($p = 0.365$) or SA (p -value = 0.714) (Figure S1 A and B, respectively, available as online-only supplementary material).

Discussion

Our findings indicate that there is a high prevalence of SI and SA among cocaine users who access health services: ranging from 27.71 to 43.59%. Similarly, a nationally representative household survey in Brazil detected a 40% and 20.8% prevalence of SI and SA, respectively, in a population of young adult and adult crack users.⁴³ However, a U.S. street outreach study found higher rates among female African American cocaine users, 32% of whom reported at least one lifetime SA.⁴⁴

In clinical samples of individuals who use psychoactive substances, the prevalence of SI ranges from 17.4 to 49.5%, while SA ranges from 20 to 39%.^{45,46} A recent study observed that the prevalence of SI and SA was 26 and 34.6%, respectively, for crack users and 15.1 and 28.3%, respectively, for alcohol users.⁴⁷ In non-clinical samples, the lifetime prevalence of SA in alcohol dependent individuals is about 40%.⁴⁸ Other psychoactive substances are also associated with suicidal behavior. The prevalence of SI and SA among heroin users ranges from 13 to 34.2% and 9.5 to 40%, respectively.⁴⁹⁻⁵³ Another study found that the SA rate among non-institutionalized adolescent ecstasy users in the USA is identical to that of other drug addicts.⁵⁴ The prevalence of SA and SI is slightly lower among marijuana users (16.5 and 31.5%, respectively).⁵⁵ Taken together, these high prevalence rates indicate that SI and SA should be addressed in both clinical and home-based studies in this population.

In fact, individuals with suicidal thoughts, attempts, or plans have a greater predisposition to commit suicide than those who have never had them.^{56,57} This is especially relevant since alcohol is consumed by 43% of the global population,⁵⁸ 54.1% of the population in the

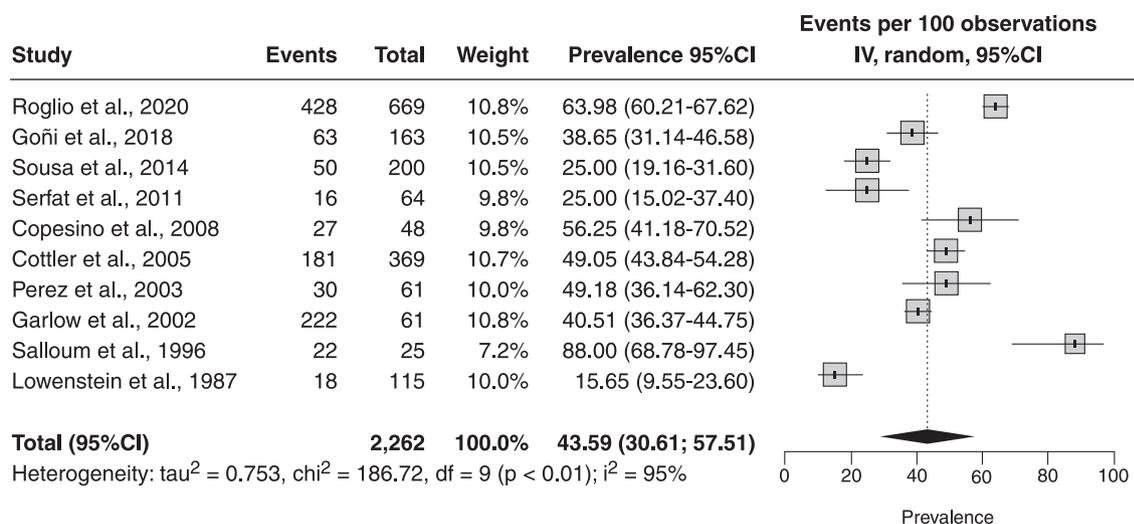


Figure 2 Meta-analysis of the prevalence of suicidal ideation. 95%CI = 95% confidence interval; df = degrees of freedom; I^2 = I-square statistic; IV = inverse variation.

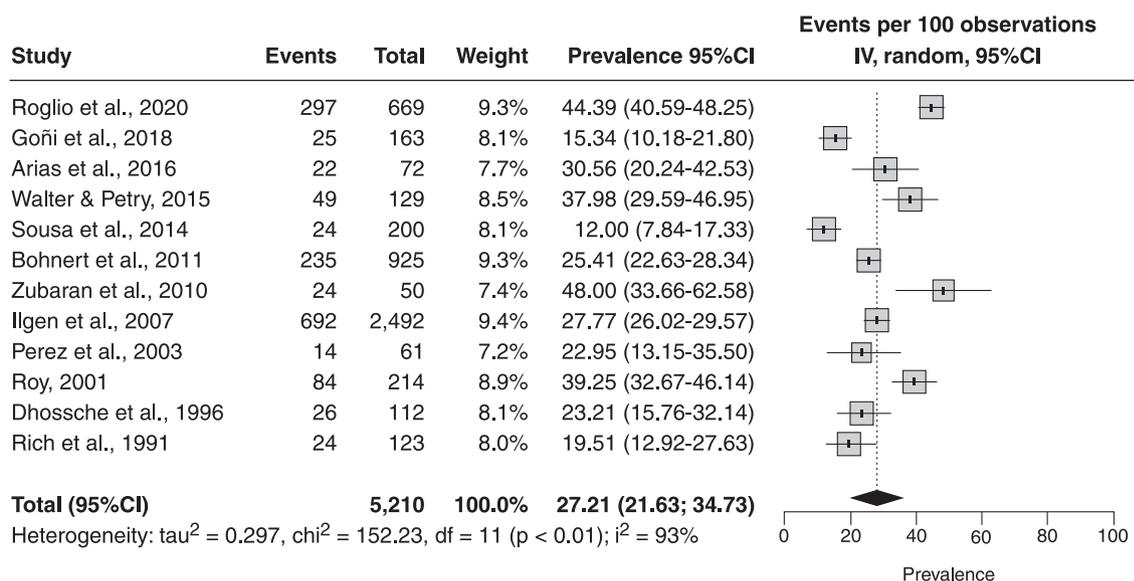


Figure 3 Meta-analysis of the prevalence of suicide attempts. 95%CI = 95% confidence interval; df = degrees of freedom; I^2 = I-square statistic; IV = inverse variation.

Americas,^{51,53} and 30.1% of the Brazilian population.⁵⁹ The prevalence is similar for marijuana (7.7%), the most consumed illicit drug, followed by cocaine (3.1%), and crack (0.3%)(III Levantamento Domiciliar Sobre o Uso de Drogas Psicotrópicas no Brasil [III LNUJ]).⁶⁰

In non-clinical and general populations, studies around the world have found a wide variation in SA prevalence, ranging from 7 to 20.3%, with a SI prevalence ranging from 2.3 to 24.66%.⁶¹⁻⁶⁵ Higher estimates have been found in clinical samples, particularly in individuals with at least one psychiatric disorder. For instance, in individuals with major depressive disorder, the SI and SA prevalence is 37.1% and 24%, respectively.^{66,67} These rates are slightly lower than those observed in cocaine users. In

individuals with other mental disorders, such as bipolar affective disorder, the prevalence of SI is very high (61%), although SA is lower (20%).⁶⁸⁻⁷⁰ The rates are also troubling in borderline personality disorder, ranging from 25 to 70% for SI and from 20 to 70% for SA.^{71,72} These rates are higher than those of the cocaine users in our meta-analysis. In patients with post-traumatic stress disorder (PTSD), SI and SA rates of 38.3% and 9.6%, respectively, were found.⁷³ Therefore, cocaine users have higher rates of suicidal behavior than PTSD patients. In addition, according to psychological autopsy reports, the prevalence of mental disorders among individuals with suicidal behavior was 69.6% in East Asia, 88.2% in North America, and 90.4% in South Asia.⁷⁴

Table 2 Subgroup analysis

| | n (%) | 95%CI | p-value | I ² (%) |
|-----------------------------|------------|-------------|---------|--------------------|
| Suicidal ideation subgroups | | | | |
| Multicenter | | | | |
| Yes | 9 (43.11) | 28.62-58.88 | 0.48 | 95 |
| No | 1 (49.05) | 43.98-54.14 | | N/A |
| Treatment regimen | | | | |
| Outpatient | 3 (55.39) | 18.29-87.32 | 0.56 | 97 |
| Inpatient | 4 (45.78) | 28.89-63.71 | | 91 |
| Both | 3 (33.06) | 16.02-56.11 | | 95 |
| Study quality | | | | |
| High | 7 (50.69) | 36.16-65.10 | 0.09 | 94 |
| Low | 3 (28.06) | 13.33-49.71 | | 91 |
| Suicide attempt subgroups | | | | |
| Multicenter | | | | |
| Yes | 2 (26.87) | 24.67-29.19 | 0.81 | 92 |
| No | 10 (27.92) | 20.53-36.74 | | 48 |
| Treatment regimen | | | | |
| Outpatient | 5 (27.14) | 20.33-35.21 | 0.52 | 79 |
| Inpatient | 4 (33.28) | 17.50-53.97 | | 95 |
| Both | 3 (23.12) | 16.65-31.17 | | 84 |
| Study quality | | | | |
| High | 9 (31.00) | 24.16-38.80 | 0.03 | 93 |
| Low | 3 (18.48) | 11.73-27.89 | | 74 |

95%CI = 95% confidence interval; I² = I-square statistic; N/A = not available.

These rates are higher than those of the cocaine users in our meta-analysis.

A systematic analysis from the Global Burden of Disease Study that used suicide mortality data between 1990 and 2016 found a 6.7% increase in the number of suicide deaths, being one of the main causes worldwide of life-years lost.⁷⁵ Another review of cohort studies found that psychoactive substance users have a 10 to 20 times greater risk of death by suicide than non-users. Most of those deaths involve heavy use of alcohol, opiates, or amphetamines.^{76,77} In addition, a meta-analysis found a 41% prevalence of suicidal behavior among older adults with a substance use disorder.⁷⁸ In a sample from England and Wales, cocaine use was also associated with 8.4% of deaths by self-injury.⁷⁹ About 20% of the drug overdose deaths in the United States involve cocaine use.⁸⁰ Suicidality and substance use increases the burden on mental health services, and have relevant social and economic consequences. A recent study with young people found that substance use and SA increase the risk of hospitalization.^{81,82} In particular, cocaine users are often stigmatized and risk neglect in medical and psychiatric care.⁸³ Since a SA is the expression of suicidal thoughts or impulses, it is visible to professionals when a patient seeks health services. On the other hand, suicidal ideation, which was quite prevalent in the findings, is less visible: health professionals must actively search for it. These data show that the most vulnerable subjects must be identified early and offered personalized care, which will help prevent health system overload. A specific instrument or protocol that is short and user-friendly would be a good way to standardize symptom screening in substance users.

Our analyses revealed high heterogeneity among the studies regarding the prevalence of suicidal behavior. To explain this phenomenon, subgroup analyses were

conducted for potentially related factors. However, neither age, sex, multicenter study design, treatment regimen, or study quality were the source of this heterogeneity (except for study quality and SA prevalence). Other characteristics associated with suicidal behavior, such as mental disorders, family support, early trauma, and impulsiveness, might help explain these results. One systematic review identified social factors related to SAs, which included conflict, marital and economic problems, and educational failures.⁸⁴ However, it should be pointed out that most studies do not provide information about the other characteristics of these individuals, hampering deeper analyses that consider the joint influence of various factors on suicidal behavior.

Our review has other limitations. Most of the included studies were cross-sectional, so cause-and-effect relationships cannot be established. Cohort and longitudinal studies are needed for more robust conclusions about whether cocaine use directly influences suicide risk or if there is a dose-response relation between cocaine use and suicide. Moreover, since our goal was to assess the SI and SA prevalence among clinical populations of cocaine users, generalizations to non-clinical samples should be approached with caution. Despite these limitations, this systematic review and meta-analysis has some strengths: a broad search strategy was applied, and several databases were analyzed to increase search sensitivity and include the largest possible number of studies. In addition, most of the studies had good methodological quality, which allowed us to calculate the prevalence of the intended outcomes. Subgroup analysis was performed, when possible, to minimize bias.

This is the first systematic review with meta-analysis to evaluate suicidal behavior in a clinical population of cocaine users, among whom a high prevalence of SI and SA were observed. Due to these troubling findings in

this vulnerable population, which are compounded by underestimation or underassessment, clinicians and even mental health professionals need greater awareness and training. Thus, it is relevant to include this condition in the development of public health policies, especially prevention strategies for this severe problem.

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Disclosure

The authors report no conflicts of interest.

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