



# Characteristics of single vs. multiple suicide attempters among adolescents: a systematic review and meta-analysis

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## Abstract

There might be differential characteristics between those who have attempted suicide once in their lifetime (single attempters) and those who have attempted suicide two or more times (multiple attempters). We aimed to identify the factors that differentiate single and multiple attempters in child and adolescents. This study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines, and the review protocol was registered in PROSPERO. We conducted a systematic literature search in three databases to identify original studies exploring the characteristics of single attempters vs. multiple attempters among adolescents. We considered a wide range for the definition of adolescent, following most recent recommendations: 10–24 years. We carried out a meta-analysis. Fourteen studies were included in the systematic review and 13 in the meta-analysis with a total sample of with a total of 4286 participants. The factors statistically significantly associated with being a multiple attempter in the meta-analysis were: anxiety disorders, depression severity, alcohol abuse, substance abuse, aggressiveness, and hopelessness. Multiple attempters have a more severe clinical profile, with greater severity of symptoms. Knowledge of the risk factors associated with being a multiple attempter could help us to predict which patients are more likely to reattempt suicide and need further monitoring and a tailored treatment. Prevention programs tailored for the adolescent population, along with identification of early risk factors, could help to prevent suicidal behavior among this vulnerable population.

**Keywords** Meta-analysis · Adolescents · Suicide · Suicide attempt · Suicide ideation

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## Introduction

Suicide is a major public health problem worldwide and one of the leading causes of unnatural death in adolescents [50]. Suicide attempts are estimated to be approximately 20 times more common than death by suicide, and they have a significant impact on quality of life and health costs. As it affects young people, suicide causes many Years of Potential Life Lost (YPLL). In the United States, the YPLL caused by suicide in 2018 were 1,344,552, a figure close to the YPLL caused by COVID-19 in 2020, which were 1,591,487 [35]. In other countries, YPLL caused by suicide were in fact higher than those caused by COVID-19 [28].

A growing number of studies in suicide research argue for the existence of suicidal phenotypes [18]. According to this consideration, suicidal behavior is not homogeneous, but comprises different population subtypes. Among the distinctions that can be made are the binomial suicide ideators vs. suicide attempters [23], high lethality vs. low lethality suicide attempts [7], impulsive vs. planned suicide attempts [32], or the distinction that we will explore in this study: single vs. multiple suicide attempters [33]. The latter distinction argues for the existence of differential characteristics between those who have attempted suicide once in their lifetime and those who have attempted suicide two or more times. The distinction between single and multiple attempters may have clinical relevance, helping us to know more about prognosis, co-morbidity, and the most appropriate approach.

Previous narrative and systematic reviews have examined some of the different suicidal phenotypes, such as those related to greater or lesser impulsivity [45], greater or lesser genetic predisposition [20], or different method used [52]. A previous systematic review by our research group explored the factors associated with the repetition of a suicide attempt in a given time frame (Méndez-Bustos et al. 2013). This review revealed heterogeneity in defining what was meant by suicide reattempt. Thus, some of the studies understood reattempt as the second suicide attempt made in a lifetime. They, therefore, considered suicide reattempters (or multiple attempters) as those who had committed more than one suicide attempt. In contrast, other studies examined a specific time frame: for example, the risk of repeating a suicide attempt 1 year after a previous suicide attempt, which we could call the suicide attempt index. However, this index suicide attempt did not necessarily have to be the person's first attempt in their life.

In this study, we have opted for a more precise definition, considering single attempters as those who have made only one suicide attempt in their lives, and multiple

attempters as those who have made two or more suicide attempts. In this systematic review and meta-analysis, we aimed to identify the factors that differentiate single and multiple attempters in the adolescent population. Our hypothesis is that multiple attempters will have a more severe risk profile, with higher prevalence of personality disorders and dysfunctional personality traits.

## Methods

This study was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [30]. The review protocol was registered in the PROSPERO database (CRD42021286599).

### Inclusion/exclusion criteria

Our inclusion criteria were:

- (i) Original studies published in peer-reviewed journals
- (ii) Studies that explored both factors associated with first suicide attempt and factors associated with suicide reattempts.
- (iii) Studies that included adolescents in their sample (either exclusively adolescents, or with data provided separately for this population). We used a wide range for the definition of adolescence, according with recent recommendations [39]: 10–24 years old.

Exclusion criteria were:

- (i) Studies that explore factors associated with suicide attempt without differentiating between first lifetime suicide attempt and suicide reattempt
- (ii) Reviews
- (iii) Theoretical studies, protocols, and other studies that do not provide measurable outcomes

There were no restrictions regarding participants' gender or ethnicity.

Further inclusion criteria for the meta-analysis were that results were provided with effect sizes and that variables of interest were assessed in at least two different studies.

### Search strategy

We conducted a systematic literature search in four databases: PubMed, Web of Science, and EMBASE. There were no restrictions by date or language. Our search terms were: (suicid\*) AND (attempt\* OR repeat) AND (factor\* OR correlat\* OR predict\*).

Experts in the field were also be consulted. The references of included studies were also be screened.

### Study selection process

Articles were selected if they were relevant to the research question and fulfilled the inclusion criteria. Titles and abstracts of the papers retrieved were screened independently by two reviewers (SAP and IPC) to identify potential studies meeting the inclusion criteria. The full text of these potentially eligible studies was independently assessed by the two reviewers. Discrepancies between reviewers was be resolved by discussion, with the participation, if necessary, of a third reviewer (APS). Level of agreement was measured by Intraclass Correlation Coefficient (ICC).

### Data extraction

Data were identified, checked, and mined by two independent reviewers (IPC, BE), and disagreements were evaluated by AA-C. We extracted the % of women, year of study, the proportion or frequencies of the psychiatric diagnostics (mood disorder, anxiety disorder, eating disorder, behavioral disorder, substance abuse and alcohol abuse) and sex in multiple and single attempters, the mean and standard deviation/error or the odds ratios of depression severity, impulsivity, aggressiveness, hopelessness, sexual abuse, alcohol abuse, drug abuse, suicidal intent, suicidal ideation and age of first suicide.

### Quality assessment

All eligible studies were reviewed and critically appraised using the Newcastle–Ottawa Scale (NOS) [43]. Aspects assessed included risk of bias, methodological design, quality of reporting, etc. Studies were considered methodologically sound if their design is appropriate to the research question, they were free of selection bias, attrition bias, and reporting bias, and the case and control groups were comparable. A minimum sample size of 10 was required.

### Data analysis

We presented a narrative synthesis of the results and carried out a meta-analysis. Analyses were performed using R.3.6.2. Due to the different way to present data in the studies, effect sizes were pre-calculated to standard mean differences (SMD). Random effects model was used to calculate the pooled effect size for all meta-analysis. Restricted maximum likelihood (RMEL) was used to calculate the heterogeneity variance  $\tau^2$ , as has been shown to be less biased in several scenarios [48]. Knapp–Hartung adjustment was used to calculate confidence interval around the pooled

effect size [24]. Between-study heterogeneity was evaluated using the Cochran's  $Q$ , prediction interval and Higgins  $I^2$  [16]. Cronbach's  $Q$   $p$  value  $< 0.050$  implies between study heterogeneity, an  $I^2$  between 25 and 50% implies low heterogeneity, an  $I^2$  between 50 and 75% implies moderate heterogeneity and  $I^2 > 75\%$  implies high heterogeneity [15]. Moreover, if prediction interval includes 0, we can be less sure that a statistically significant result will continue to be statistically significant in future studies due to heterogeneity. When heterogeneity was low to high, we performed outlier diagnostics and influence analyses to detect the studies that could increase this heterogeneity [49]. Publication bias was assessed using funnel plots. Data were interpreted through a narrative discussion of the main findings.

## Results

### Results of the bibliographical search

The initial search revealed 47,869 results. Following initial screening, full-text revision, and selection process, 14 articles were finally included in the review. Figure 1 shows the PRISMA flow chart of the bibliographical search. Intraclass correlation coefficient (ICC) among reviewers was 85.56 (95% CI 81.58%–88.96%). Thirteen articles fulfilled further selection criteria and were included in the meta-analysis. One study (Chen et al. 2013) was not included in the meta-analysis because the procedure did not allow to differentiate well between single and multiple attempters. However, we included it in the qualitative analysis. The meta-analysis had a total of 4286 participants of whom 1579 were multiple suicide attempters, and 2707 single suicide attempters. The average score in the NOS scale was 6.27 for case–control studies and 7.5 for cohort studies. ICC between the two NOS scale raters was 0.959 (excellent agreement).

### Characteristics of the reviewed studies

Ten of the reviewed studies had a cross-sectional design, while three of them had a longitudinal design—although some of them included both cross-sectional and longitudinal data—. Minimum age explored in the studies was 11 years old [1], while the maximum age was 24 (Chen et al. 2013). The funnel plots showed a symmetric distribution for all the studied variables (see supplementary materials) showing absence of publication bias. Tables 1 and 2 present a summary of the characteristics and main findings of the reviewed studies. Figures 2 and 3 present the main results of the meta-analysis. Below, we present a summary of the results organized by risk factor explored.

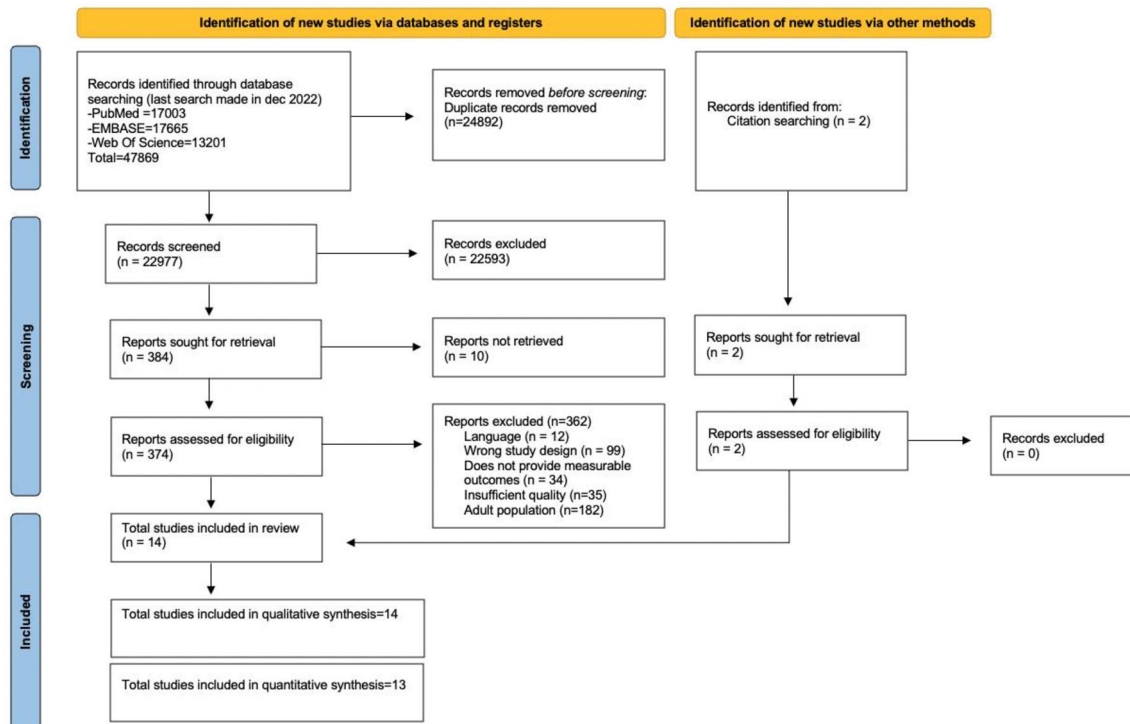


Fig. 1 PRISMA flow chart

## Age and age at suicide attempt/suicidal ideation

Four studies included the age during the study for multiple and single attempters, showing non-significant results in the meta-analysis (SMD = 0.008, 95% CI [-0.29, 0.31],  $p < 0.932$ ; supplementary material). Studies were homogeneous ( $Q = 1.38$ ,  $p < 0.709$ ,  $I^2 = 0\%$ ).

Two studies included the age at first suicide attempt to compare multiple and single attempters [1, 10]. Regarding suicidal ideation, two studies compared this variable between multiple and single attempters [8, 26]. Despite the limited number of studies to perform a meta-analysis for both variables, we tested their pooled effect size due to the importance of these variables in suicide research.

Pooled effect size for age at first suicide attempt showed non-significant differences between multiple attempters and single attempters in the meta-analysis (SMD = -0.489, 95% CI [-2.35, 1.37],  $p < 0.185$ ; supplementary material). Studies were homogeneous ( $Q = 0.42$ ,  $p < 0.516$ ,  $I^2 = 0\%$ ). For suicidal ideation, there were significant effects showing multiple attempters higher suicidal ideation than single attempters (SMD = 0.399, 95% CI [0.34, 0.46],  $p < 0.007$ ; supplementary material). Studies were homogeneous ( $Q = 0$ ,  $p < 0.981$ ,  $I^2 = 0\%$ ).

## Gender

Five studies compared if the proportion of women was different between multiple and single attempters [1, 9, 10, 25, 47].

Gender showed non-significant results in the comparison multiple attempters and single attempters in the meta-analysis (SMD = 0.082, 95% CI [-0.11, 0.27],  $p < 0.291$ ; Fig. 2A). Studies were homogeneous ( $Q = 0.86$ ,  $p < 0.931$ ,  $I^2 = 0\%$ ).

## Mood disorders

Four studies had data on mood disorders for multiple and single attempters [11, 13, 26, 47]. All studies used clinical interviews to perform their diagnostic. For instance, [11] carried out a cross-sectional study in which they analyzed a sample of patients aged 12–18 years who presented to the emergency department in the context of a suicide attempt. 45 of them were first-time attempters and 50 were reattempters. They found that the group of multiple attempters were more like to have a diagnosis of affective disorder ( $\chi^2 = 13.25$ ,  $p < 0.01$ ).

**Table 1** Main results of the reviewed studies: cross-sectional studies

Study	Country	Sample	Main findings
[1]	France	302 people (83% female) aged 11–17 y hospitalized after an SA, 219 with BPD. Ethnicity NR	Factors statistically significantly associated with MA vs. SA: NSSI (OR = 2.87, $p < 0.001$ ) Functioning (OR = 0.97, $p = 0.006$ ) Age at first attempt (OR = 0.70, $p = 0.013$ ) Non-significant factors: anxiety, depression, ADHD, impulsivity, substance abuse; suicidal severity; gender; mother's education; negative life events Statistically significant differences between MA and SA in: Psychosis or personality disorder (21.5% vs. 35.7%, $p < 0.01$ ) Family with over four children (43.8% vs. 61.1%, $p < 0.01$ ) Family history of alcohol abuse (27% vs. 2%, $p < 0.01$ ) School problems (24.1% vs. 42%, $p < 0.01$ ) Family problems (27.6% vs. 40.6%, $p < 0.01$ ) Depressive symptoms (25.6% vs. 45.4%, $p < 0.01$ ) Factors statistically significantly associated with MA vs. SA: Age of first attempt (OR = 0.33, $p = 0.001$ ) Treatment following attempt (OR = 0.28, $p = 0.028$ )
[9]	France	537 people (77% female) aged 14–19 hospitalized after a suicide attempt Ethnicity: SA: 89% Caucasian, 5.4% North African, 5.6% Other MA: 86.6% Caucasian, 6.4% North African, 7.0% Other	Factors statistically significantly associated with MA vs. SA: Mood disorders (DISC) ( $\chi^2 = 13.25$ , $p < 0.01$ ) Disruptive behavior disorder ( $\chi^2 = 8.52$ , $p < 0.01$ ) Non-significant factors: alcohol use disorder, cannabis use Factors statistically significantly associated with MA vs. SA: Less success in school ( $t = 3.43$ , $df = 38.35$ , $p < 0.01$ ) Less school attendance ( $t = 3.56$ , $df = 36.34$ , $p < 0.01$ ) Greater difficulty in the modulated expression of anger ( $t = 3.78$ , $df = 38.34$ , $p < 0.01$ ) Greater dysphoria ( $t = 1.72$ , $df = 38.34$ , $p < 0.05$ ) Number of life stressors ( $t = 2.52$ , $df = 36.33$ , $p < 0.05$ ) Greater suicide intent ( $t = 2.24$ , $df = 40.36$ , $p < 0.05$ ) Factors statistically significantly associated with MA vs. SA: Greater prevalence of affective disorders ( $p < 0.05$ ) Smaller prevalence of adjustment disorders ( $p < 0.05$ ) Non-significant factors: prevalence of anxiety disorders, substance use, conduct/oppositional disorders, and ADHD
[10]	USA	95 people (81% female) aged 13–18 hospitalized after a suicide attempt. Ethnicity: 83.2% Caucasian, 3.2% African American, 2.1% Native American, 2.1% Asian, 9.5% other	Factors statistically significantly associated with MA vs. SA: Age of first attempt (OR = 0.33, $p = 0.001$ ) Treatment following attempt (OR = 0.28, $p = 0.028$ )
[11]	USA	121 people (85% female) aged 12–18 attended at the Emergency Department after a suicide attempt. Ethnicity: 68.6% Caucasian, 10.7% Hispanic, 11.6% African American, 9.1% Other	Factors statistically significantly associated with MA vs. SA: Mood disorders (DISC) ( $\chi^2 = 13.25$ , $p < 0.01$ ) Disruptive behavior disorder ( $\chi^2 = 8.52$ , $p < 0.01$ ) Non-significant factors: alcohol use disorder, cannabis use Factors statistically significantly associated with MA vs. SA: Less success in school ( $t = 3.43$ , $df = 38.35$ , $p < 0.01$ ) Less school attendance ( $t = 3.56$ , $df = 36.34$ , $p < 0.01$ ) Greater difficulty in the modulated expression of anger ( $t = 3.78$ , $df = 38.34$ , $p < 0.01$ ) Greater dysphoria ( $t = 1.72$ , $df = 38.34$ , $p < 0.05$ ) Number of life stressors ( $t = 2.52$ , $df = 36.33$ , $p < 0.05$ ) Greater suicide intent ( $t = 2.24$ , $df = 40.36$ , $p < 0.05$ ) Factors statistically significantly associated with MA vs. SA: Greater prevalence of affective disorders ( $p < 0.05$ ) Smaller prevalence of adjustment disorders ( $p < 0.05$ ) Non-significant factors: prevalence of anxiety disorders, substance use, conduct/oppositional disorders, and ADHD
[12]	USA	81 people aged 12–18 hospitalized after a suicide attempt. Ethnicity NR	Factors statistically significantly associated with MA vs. SA: Age of first attempt (OR = 0.33, $p = 0.001$ ) Treatment following attempt (OR = 0.28, $p = 0.028$ )
[13]	USA	269 hospitalized people (73% female) aged 12–19. Ethnicity: 80% Caucasian, 17% African American, 2% Other	Factors statistically significantly associated with MA vs. SA: Age of first attempt (OR = 0.33, $p = 0.001$ ) Treatment following attempt (OR = 0.28, $p = 0.028$ )
[25]	Finland	406 people (72% female) aged 15–19 hospitalized after a suicide attempt. Ethnicity NR	Factors statistically significantly associated with MA vs. SA: Employment ( $\chi^2 = 14.2$ , $p < 0.001$ ) History of psychiatric treatment ( $\chi^2 = 97.3$ , $p < 0.01$ ) Integration of the family ( $\chi^2 = 12.3$ , $p < 0.001$ ) Level of adaptive functioning (Axis V, DSM-III) ( $\chi^2 = 34$ , $p < 0.001$ ) Level of functioning and symptoms (GAS) ( $\chi^2 = 62.9$ , $p < 0.001$ ), criminality ( $\chi^2 = 7.27$ , $p < 0.05$ ), excessive use of alcohol ( $\chi^2 = 27.9$ , $p < 0.001$ ), medicines abuse ( $\chi^2 = 32.9$ , $p < 0.001$ ), drug abuse ( $\chi^2 = 29$ , $p < 0.001$ ) Non-significant factors: gender

Table 1 (continued)

Study	Country	Sample	Main findings
[26]	USA	59 hospitalized females aged 13–17. Ethnicity: No attempts: 90.9% Caucasian, 9.1% African American SA: 73.3% Caucasian, 20% African American, 6.7% Hispanic MA: 77.3% Caucasian, 9.1% African American, 4.5% Hispanic, 9.1% Other	Factors statistically significantly associated with MA vs. SA: Aggression (LHA): mean scores for SA = 17.3 (SD = 7.4); mean scores for MA = 22.7 (SD = 7.2); $p = 0.033$ Depression (BDI) mean scores for SA = 13.9 (SD = 6.5); mean scores for MA = 24 (SD = 9.7); $p = 0.001$ Non-significant factors: impulsivity, suicide intent, and suicide ideation
[36]	Lebanon	16,664 public high school students (50% females). Ethnicity: 88% Caucasian, 2% African American, 2% Hispanic, 3% Asian American, 3% Native American, 2% missing data	Factors statistically significantly associated with MA vs. SA: Weight (OR = 3.56, $p < 0.001$ ) Violence (OR = 3.18, $p < 0.001$ ) Sexual assault (OR = 3.49, $p < 0.001$ ) Physical assault (OR = 2.73, $p < 0.001$ ) Depressed mood (OR = 7.91, $p < 0.001$ ) Tobacco use (OR = 2.52, $p < 0.001$ ) Alcohol use (OR = 2.47, $p < 0.001$ ) Cannabis use (OR = 2.50, $p < 0.001$ ) Hard drugs use (OR = 3.57, $p < 0.001$ ) Sexual risk taking (OR = 2.33, $p < 0.001$ )
[42]	Israel	245 hospitalized people (50% female) aged 12–18. Ethnicity NR	Factors statistically significantly associated with MA vs. SA: General aggression (SPS) (mean scores for MA = 5.56, SD = 2.66, mean scores for SA = 3, SD = 2.43, $p = 0.026$ ) Destructiveness (SPS) (mean scores for MA = 1.61, SD = 0.51); mean scores for SA = 1.24, SD = 0.44, $p = 0.009$ ) Violence (SPS) (mean scores for MA = 1.67, SD = 1.49; mean scores for SA = 1.94, SD = 1.52, $p = 0.025$ ) Antisocial behavior (SPS) (mean scores for MA = 1.61, SD = 1.46; mean scores for SA = 0.84, SD = 1.23, $p = 0.025$ ) Non-significant differences in depression, anxiety, anger, and impulsivity
[47]	USA	194 hospitalized people (62% female) aged 12–17. Ethnicity: 90.2% Caucasian, 3.1% Hispanic, 2.1% Asian, 2.1% bi or multiracial, 0.5% black, 2% other	Non-significant differences in depression, anxiety, anger, and impulsivity symptoms, and maternal and paternal attachment

*BPD* borderline personality disorder, *HR* hazard ratio, *MA* multiple attempts, *NSSI* non-suicidal self-injury, *OR* odds ratio, *SA* single attempters, *LHA* Life History of Aggression, *BDI* Beck Depression Inventory, *DISC* Diagnostic Interview Schedule for Children, *ADHD* Attention-Deficit / Hyperactivity Disorder, *SPS* Suicide Potential Scale, *DSM* Diagnostic and Statistical Manual of Mental Disorders, *GAS* Global Assessment Scale, *SD* standard deviation

**Table 2** Main results of the reviewed studies: longitudinal studies

Study	Country	Follow-up period	Sample	Main findings
Chen et al. (2013)	Taiwan	12 months	7313 people (44% female) aged 15–24 attended for suicidal behavior	Factors statistically significantly associated with MA vs. SA: In males: Near poverty (HR=0.76, $p < 0.01$ ) Poverty (HR=0.46, $p < 0.01$ ) Treatment for mental disorders (HR=0.80, $p < 0.05$ ) In females: Poverty (HR=1.58, $p < 0.05$ ) Treatment for anxiety disorders (HR=0.68, $p < 0.001$ ) After the first attempt, 33% of males and 23% of females reattempted during the following 12 months. Maximum risk for the first reattempt was during the second to fourth month after the first attempt
[8]	USA	12 months	338 people (71% female) aged 13–17 hospitalized for suicidal behavior	Statistically significant differences between MA and SA in: Suicide ideation (SIQ-JR): mean scores for MA=51.98, SD=19.92; mean scores for SA=43.92, SD=20.58, $p < 0.001$ Statistically non-significant difference in depression and connectedness
[14]	UK	12 months	45 people (84% female) aged 15–19 hospitalized after a suicide attempt	Factors statistically significantly associated with MA vs SA: Depression (BDI) ( $t=3.81$ , $p < 0.001$ ) Hopelessness (BHS) ( $t=3.48$ , $p < 0.01$ ) State anger (SSTAI) ( $t=1.90$ , $p < 0.07$ ) Self-concept (SC-Q) ( $t=2.64$ , $p < 0.05$ ), problem-solving (SRPSI) ( $t=2.52$ , $p < 0.05$ ) Problem Solving (MEPS) ( $t=1.99$ , $p < 0.06$ ) Non-significant factors: suicidal intent, impulsivity, and trait anger (SSTAI)

*BPD* borderline personality disorder, *HR* hazard ratio, *MA* multiple attempters, *NSSI* non-suicidal self-injury, *OR* odds ratio, *SA* single attempters, *BHS* Beck Hopelessness Scale, *SSTAI* State-Trait Anxiety Inventory, *MEPS* Means End Problem Solving, *SC-Q* Self-Concept Questionnaire, *SRPSI* Self-Regulation Strategy Inventory

Non-significant results were found for mood disorders in the meta-analysis (SMD=0.56, 95% CI [-0.65, 1.77],  $p < 0.237$ ; Fig. 1A). Studies had low heterogeneity ( $Q=4.36$ ,  $p < 0.223$ ,  $I^2=31.2\%$ ).

### Depression severity

Seven studies included a measure of depression severity to compare multiple and single attempters, six cross-sectional [1, 8, 11, 26, 36, 42] and one longitudinal study [14]. Four studies used the BDI, one the CDRS, one the CES-D and one and one a self-reported questions from a national survey.

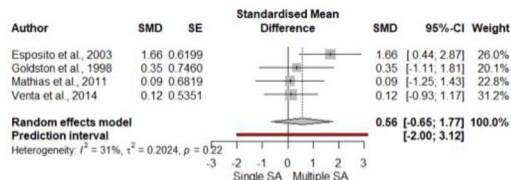
In the meta-analysis, multiple attempters showed statistically significant higher depression severity than single attempters (SMD=0.515, 95% CI [0.17, 0.86],  $p < 0.011$ ; Fig. 2A). Studies were homogeneous ( $Q=5.71$ ,  $p < 0.456$ ,  $I^2=0\%$ ) but 95% prediction interval includes 0. When removing the longitudinal study, results became more

statistically significant (SMD=0.654, 95% CI [0.28, 1.03],  $p < 0.009$ ) and the prediction interval did not include 0 (95% CI [0.01, 1.30]). Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,5}=1.29$ ,  $p < 0.307$ ), % of women ( $F_{1,5}=0.09$ ,  $p < 0.770$ ) or the depression scale used ( $F_{3,3}=2.31$ ,  $p < 0.256$ ).

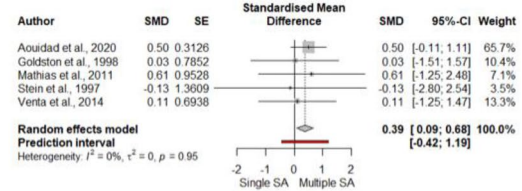
### Anxiety disorders

Five studies included a measure of anxiety to compare multiple and single attempters. All studies evaluated diagnosis using a structured interview, such as K-SADS [1, 26, 42] ISC [13] or C-DISC [47]. For instance, [1] conducted a cross-sectional study in a sample of 302 adolescents aged 11–17 years admitted after a suicide attempt. Among patients with BPD, there were no statistically significant differences in terms of frequency of anxiety disorders between

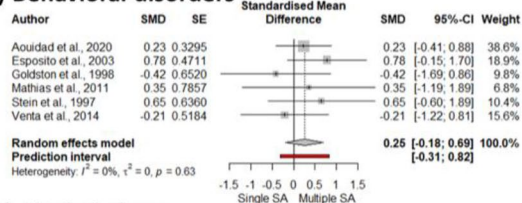
## A) Mood disorder



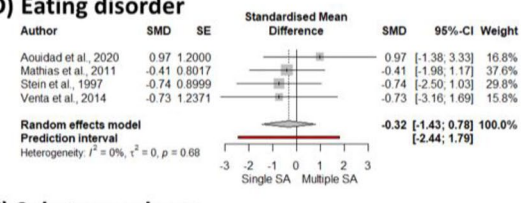
## B) Anxiety disorder



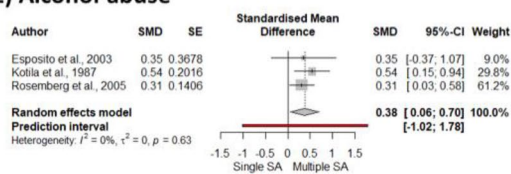
## C) Behavioral disorders



## D) Eating disorder



## E) Alcohol abuse



## F) Substance abuse

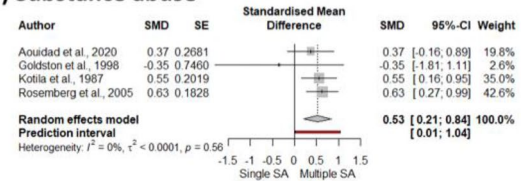
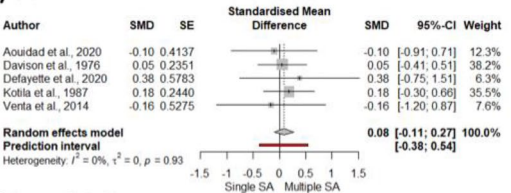
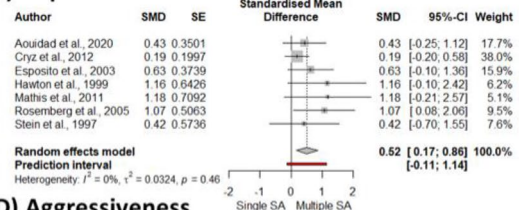


Fig. 2 Forest plots for the comparison between single and multiple attempters for the psychiatric diagnoses: **A** mood disorders, **B** anxiety disorders, **C** behavioral disorders, **D** eating disorders, **E** alcohol abuse, and **F** substance abuse

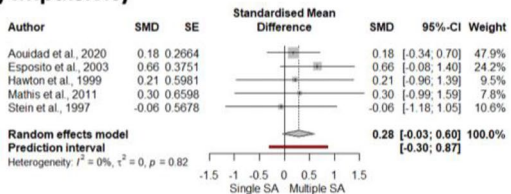
## A) Sex



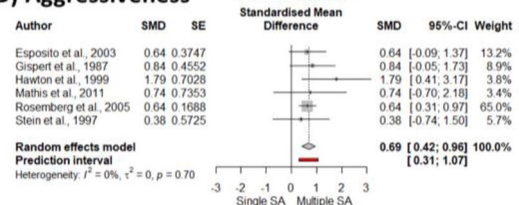
## B) Depression



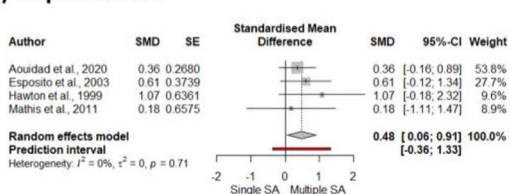
## C) Impulsivity



## D) Aggressiveness



## E) Hopelessness



## F) Suicidal intent

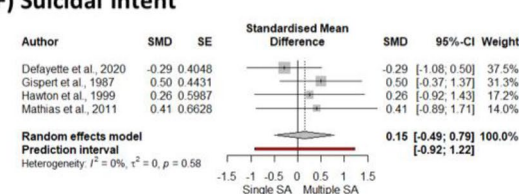


Fig. 3 Forest plots for the comparison between single and multiple attempters for the sociodemographic and the clinical risk factors: **A** sex, **B** depression severity, **C** impulsivity, **D** aggressiveness, **E** hopelessness, and **F** suicidal intent

multiple and single attempters ( $p = 0.062$ ). Among patients without BPD, multiple attempts were more likely to present with an anxiety disorder and the difference was statistically significant ( $OR = 3.75$ ,  $p = 0.018$ ).

In the meta-analysis, anxiety disorders were statistically significant for the comparison multiple attempters vs single attempters ( $SMD = 0.387$ ,  $95\% \text{ CI [0.09, 0.68]}$ ,  $p < 0.022$ ; Fig. 1B). Studies were homogeneous ( $Q = 0.70$ ,  $p < 0.952$ ,



$I^2=0\%$ ) but the prediction interval includes 0 (see Fig. 1B). Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,3}=5.33$ ,  $p<0.104$ ) or the scale used ( $F_{2,2}=2.09$ ,  $p<0.323$ ). However, meta-regression showed a statistically significant effect for the % of women in the study ( $\beta=0.02$ ,  $F_{1,3}=11.29$ ,  $p<0.044$ ).

### Eating disorders

Four studies measured eating disorders in multiple and single attempters [1, 26, 42, 47]. All studies used clinical interviews to perform the diagnostic.

Non-significant results were found for behavioral disorders in the meta-analysis (SMD = -0.32, 95% CI [-1.43, 0.78],  $p<0.419$ ; Fig. 1D). Studies were homogeneous ( $Q=1.50$ ,  $p<0.683$ ,  $I^2=0\%$ ).

### Alcohol abuse

Three studies included a measure of alcohol abuse to compare multiple and single attempters. [11] used a self-rated questionnaire, the alcohol-dependence questionnaire, [25] the diagnostic according to psychiatrics criteria and Rosemberg et al. (2005) used some self-reported questions from a national survey. For instance, [36] conducted a cross-sectional analysis of 16,664 adolescents aged 13–18 years who attended public school. Multiple attempters had higher odds for alcohol abuse (OR = 2.47, 95% CI 2.0–3.0) among many other associated factors.

Results of the meta-analysis showed that multiple attempters had statistically significant higher alcohol abuse than single attempters (SMD = 0.382, 95% CI [0.07, 0.70],  $p<0.036$ ; Fig. 1E). Studies were homogeneous ( $Q=0.92$ ,  $p<0.631$ ,  $I^2=0\%$ ) but 95% prediction interval includes 0. Mixed-effect meta-regression was performed showing a statistically significant negative effect for year of publication ( $F_{1,1}=586.02$ ,  $p<0.026$ ,  $\beta=-0.01$ ), but non-significant effects for % of women ( $F_{1,1}=1.04$ ,  $p<0.494$ ). Differences in scales were not tested because insufficient number of studies.

### Other substances abuse

Four studies included a measure of other substances abuse to compare multiple and single attempters. [1] used the self-questionnaire DEP-ADO, [13] the diagnostic according to the ISC interview, [25] the diagnostic according to psychiatric criteria and Rosemberg et al. (2005) some self-reported questions from a national survey.

In the meta-analysis, multiple attempters had statistically significant higher substance abuse than single attempters (SMD = 0.526, 95% CI [0.21, 0.84],  $p<0.013$ ; Fig. 1F).

Studies were homogeneous ( $Q=2.08$ ,  $p<0.555$ ,  $I^2=0\%$ ) and 95% prediction interval does not include 0. Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,2}=0.12$ ,  $p<0.761$ ) and % of women ( $F_{1,2}=1.03$ ,  $p<0.416$ ).

### Behavioral disorders

Six studies measured behavioral disorders in multiple and single attempters [1, 11, 13, 26, 42, 47]. All studies used clinical interviews to perform the diagnosis.

Non-significant results were found for behavioral disorders in the meta-analysis (SMD = 0.254, 95% CI [-0.18, 0.69],  $p<0.197$ ; Fig. 1C). Studies were homogeneous ( $Q=3.48$ ,  $p<0.627$ ,  $I^2=0\%$ ).

### Aggressiveness

Six studies included a measure of aggressiveness to compare multiple and single attempters, five cross-sectional [11, 12, 26, 36, 42] and one longitudinal [14]. All the studies used different scales to measure aggressiveness except [11] and [14] who used the STAXI.

In the meta-analysis, multiple attempters showed statistically significant higher aggressiveness than single attempters (SMD = 0.688, 95% CI [0.42, 0.96],  $p<0.001$ ; Fig. 1D). Studies were homogeneous ( $Q=2.97$ ,  $p<0.704$ ,  $I^2=0\%$ ) and 95% prediction interval does not include 0. Even when removing the longitudinal study, results continued to be statistically significant (SMD = 0.672, 95% CI [0.34, 1.01],  $p<0.005$ ). Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,4}=0.28$ ,  $p<0.619$ ), % of women ( $F_{1,4}=0.59$ ,  $p<0.497$ ) or the anger scale used ( $F_{1,4}=0.14$ ,  $p<0.945$ ).

### Impulsivity

Five studies included a measure of impulsivity to compare multiple and single attempters, four cross-sectional [1, 11, 26, 42] and one longitudinal [14]. Any study used the same scale to measure impulsivity.

In the meta-analysis, multiple attempters showed a trend towards higher impulsivity than single attempters, but the results did not reach statistical significance (SMD = 0.28, 95% CI [-0.03, 0.60],  $p<0.068$ ; Fig. 2C). Studies were homogeneous ( $Q=1.55$ ,  $p<0.818$ ,  $I^2=0\%$ ). When removing the longitudinal study [14] results became even more non-significant (Hedges'  $g=0.29$ , 95% CI [-0.15, 0.73],  $p<0.126$ ). Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,3}=0.23$ ,  $p<0.663$ ) and % of women ( $F_{1,3}=1.16$ ,  $p<0.359$ ).

## Hopelessness

Four studies included a measure of hopelessness to compare multiple and single attempters, three cross-sectional [1, 11, 26] and one longitudinal [14]. Three of them used the Beck Hopelessness Scale, when one used the Hopelessness scale for children. For instance, [14] conducted a 1-year longitudinal follow-up study among 45 adolescents aged 13–18 years who presented to hospital after a drug overdose. Multiple attempters had higher levels of hopelessness ( $t = 3.48$ ,  $p < 0.01$ ) among other characteristics.

In the meta-analysis, multiple attempters showed statistically significant higher hopelessness than single attempters (SMD = 0.482, 95% CI [0.06, 0.91],  $p < 0.037$ ; Fig. 2E). Studies were homogeneous ( $Q = 1.39$ ,  $p < 0.709$ ,  $I^2 = 0\%$ ), however, 95% prediction interval includes 0. When removing the longitudinal study, results continued to be statistically significant (SMD = 0.419, 95% CI [0.001, 0.84],  $p < 0.049$ ). Mixed-effect meta-regression was performed showing non-significant effects for year of publication ( $F_{1,2} = 3.12$ ,  $p < 0.219$ ), % of women ( $F_{1,2} = 0.17$ ,  $p < 0.721$ ) or the hopelessness scale used ( $F_{1,2} = 0.27$ ,  $p < 0.657$ ).

## Sexual abuse

Three studies measured sexual abuse in multiple and single attempters [1, 26, 36]. One of the studies used the negative life events sub-scale of sexual abuse, other used the K-SADS psychiatric interview to evaluate sexual abuse and the last one some questions of a national survey.

Non-significant results were found for sexual abuse in the meta-analysis (SMD = 0.209, 95% CI [-0.57, 0.99],  $p < 0.367$ ; supplementary material). Studies were homogeneous ( $Q = 2.38$ ,  $p < 0.305$ ,  $I^2 = 15.9\%$ ).

## Suicidal intent

Four studies included a measure of suicidal intent to compare multiple and single attempters, three cross-sectional [10, 12, 26] and one longitudinal [14]. Two of them used the suicidal intent scale, when one used the clinical general impression, and one used the suicidal intent sub-scale from the longitudinal interval follow-up evaluation.

Meta-analysis for suicidal intent showed non-significant differences between multiple attempters and single attempters (SMD = 0.149, 95% CI [-0.49, 0.79],  $p < 0.513$ ; Fig. 2F). Studies were homogeneous ( $Q = 1.98$ ,  $p < 0.577$ ,  $I^2 = 0\%$ ). When removing the longitudinal study, results continued to be non-significant (SMD = 0.134, 95% CI [-1.01, 1.29],  $p < 0.658$ ).

## Discussion

### Summary of results

In this systematic review with meta-analysis, we have found several factors that could help us to differentiate between multiple attempters and single attempters in adolescents, and that could, therefore, guide us in the identification of a more severe profile of patients who are more likely to make several suicide attempts during their lifetime. Thus, in the meta-analysis, we found that, in a statistically significant way, multiple attempters are characterized by greater depression severity, higher frequency of anxiety disorders, higher abuse of alcohol and other substances, higher aggressiveness, higher hopelessness, and higher suicidal ideation. There was also a non-significant trend towards higher impulsivity.

### Comparison with previous literature

There is limited research performed in the adolescent population regarding the characteristics of suicide reattempters. In a previous systematic review focused on the adult population, the authors found several factors associated with repetition of suicide attempt, including unemployment, single/separated/widowed marital status, family history of suicidal behavior, psychiatric diagnosis, suicidal ideation, and stressful life events [27]. However, some of these factors, such as unemployment of marital status, are of limited interest in the adolescent population. The only factor where this previous review and our review concur is that the multiple attempters appear to have a higher suicidal ideation. However, there are several differences between our review and this previous systematic review that preclude a direct comparison of results, including child and adolescent population in our review vs. adult population in the previous review, and the heterogeneity in the operational definition of suicide reattempt in the previous review.

### Potential underlying mechanisms

The risk factors associated with multiple attempters generally indicate a patient profile of greater clinical severity—greater depression severity, higher frequency of anxiety disorders, higher abuse of alcohol and other substances, higher aggressiveness, higher hopelessness, and higher suicidal ideation. We should, however, bear in mind that some of these characteristics could also be associated with typical adolescent risk-taking behaviors, such as higher aggressiveness and substance abuse [5].

The integrated motivational-volitional model of suicide (IMV) [31] describes a typical trajectory of suicidal

behavior and points to certain variables involved in each phase. However, this model, as well as other models of suicidal behavior such as the three-step theory [46], focus on the steps from baseline to ideation and from ideation to attempt, and do not consider another important step: from attempt to reattempt. It is possible that the determinants of becoming a multiple suicide attempter overlap with those of moving from ideation to attempt. Thus, after a first attempt, the individuals may return to a phase of relative stability and advance to suicidal ideation at a certain point (a repetition of the motivational phase) or persist in their suicidal ideation and from this point advance once again to a suicide attempt (a repetition of the volitional phase). In this sense, several of the factors that we found associated with being a multiple attempter overlap with those indicated present in the MVI, such as depression severity of hopelessness (in the motivational phase), or aggressiveness and substance abuse (in the volitional phase). Specifically, for the latter two variables, studies have found that aggressiveness may be a key factor in differentiating suicide attempters vs. non-attempters, at least in adult populations [22]. For its part, substance abuse is a well-known risk factor for suicide, both in adult [51] and adolescent [34] populations.

However, it may also be the case that the progression to a situation of multiple attempts is an additional step that is not reflected in the usual models and requires its own conceptualization. One variable that is exclusive to the transition from attempt to reattempt is a previous suicide attempt. Several studies have shown that the number of previous attempts is a risk factor both for suicide reattempt [17] and for death by suicide [4]. Prior suicide attempts, as well as previous self-harm in general, may decrease fearlessness about death and facilitates further and progressively more lethal self-harm.

### Implications for clinical practice

In the assessment after a suicide attempt, it is important to identify risk factors that could indicate a higher probability of repetition of the attempt throughout life. Thus, in this study, we have found factors that indicate that reattempts are more likely in the context of a more severe clinical profile, with greater severity of symptoms such as depression, suicidal ideation, aggressiveness or hopelessness, and that certain comorbidities, such as substance abuse, increase this risk.

The likelihood of recurrence after a first attempt varies considerably depending on the study and the time frame studied, but the literature seems to agree that the greatest risk of recurrence accumulates in the three to six months following an attempt. For instance, [17] followed-up a group of 371 people after a suicide attempt and found that 19% of participants reattempted and that 60% of these reattempts happened during the first 6 months. Similarly, [37] found

that about 40% of suicide attempters reattempted suicide in the three months after discharge.

At the far end of the group of multiple attempters are the major repeaters, people who have attempted suicide at least five times in their lifetime. One study showed some characteristics of this subpopulation, including female sex, lower educational level, higher frequency of anorexia nervosa, higher substance abuse, and higher levels of anger [3]. Some of these factors are the same that we found for multiple attempters, namely anger—a construct similar to aggressiveness—and substance abuse.

The repetition of multiple non-lethal attempts might lead us to believe that this population has a lower risk of death. In fact, studies show the opposite trend: suicide reattempters have a higher risk of death by suicide [6, 40] and almost half of suicide deaths occurred in people who had previously attempted suicide [44]. Moreover, beyond the increased risk of death, suicide attempts generate a loss in the quality of life of the person and are associated with large health care costs [21, 38].

The development of tailored treatment plans in the multiple attempter population may help to prevent the risk of reattempt. Available interventions include the safety planning intervention (SPI), a set of strategies for coping with a suicidal crisis, initially designed by Stanley and Brown [41]. The SPI can be in paper format or, more recently, in a digital version [2]. This intervention requires some prior knowledge of the person about the nature of their suicidal crises and how best to cope with them. For example, the patients are asked to identify what are their warning signs that may alert them to the advent of a suicidal crisis, or what coping strategies tend to work best for them in order to deal with it. Thus, the SPI is appropriate for people who have previously experienced one or more suicidal crises. Recently, the SPI has also been trialed in adolescents with promising results [19, 29].

### Limitations

Our findings need to be interpreted considering some limitations. First, not all the studies could be included in the meta-analysis. The study from [14] was removed from the meta-analysis after performing a posteriori sensitivity analysis. Two studies included the age at first suicide attempt to compare multiple and single attempters [1, 10]. Regarding suicidal ideation, two studies compared this variable between multiple and single attempters [8, 26]. Despite the limited number of studies to perform a meta-analysis for both variables, we tested their pooled effect size due to the importance of these variables in suicide research. Finally, we did not find eligible studies exploring potential relevant risk factors, such as socioeconomic background, ethnicity, or family history of suicidal behavior.

## Conclusions

Suicidal behavior is a complex phenomenon that requires a nuanced study of its different phenotypes. In this systematic review with meta-analysis, we found that the subpopulation of adolescent multiple attempters is associated with different characteristic risk factors. Knowledge of these risk factors could help us to predict which adolescent patients are more likely to reattempt suicide and therefore, need further monitoring and tailored treatment. Prevention programs tailored for the adolescent population, along with identification of early risk factors, could help to prevent suicidal behavior among this vulnerable population.

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**Data Availability** Data are available upon request.

## Declarations

**Conflict of interest** The author declares that have no conflict of interest.

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