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Internalizing and externalizing symptoms and suicidal behavior in young people: a systematic review and meta-analysis of longitudinal studies

Internalizing and externalizing symptoms and suicidality in youth

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ABSTRACT

Objective: To assess internalizing and externalizing symptoms as risk factors for suicidal behavior and suicide among adolescents and young adults.

Method: We conducted a systematic review of articles published until January 2017. We identified 26883 potential papers; 1701 full text articles were assessed for eligibility, of which 1479 were excluded due to methodological reasons. Diverse meta-analyses were performed for each group of symptoms. Odds ratios (ORs) and 95% confidence intervals (95% CI) or beta coefficients for categorical variables, and effect size (ES) were calculated for continuous variables.

Results: Finally, 41 studies were included, involving participants aged 12–26 years for a systematic review, and 24 articles were included for meta-analysis. The meta-analysis showed that youths with any internalizing (ES = 0.93) or externalizing symptoms (ES = 0.76 and OR = 2.59) were more likely to attempt suicide in future. This effect was also seen in

depression symptoms (OR = 6.58 and ES = 1.00), legal problems (OR = 3.36), and anxiety (ES = 0.65).

Conclusion: Reported internalizing and externalizing symptoms are predictors of suicide behavior in young people; therefore, the detection and management of these symptoms in young populations could be a crucial strategy for preventing suicidality in this group.

Keywords: Internalizing symptoms, externalizing symptoms, suicidal behavior, youths, systematic review, meta-analysis

Summations

- For the first time, this systematic review provides summary information about the role of internalizing and externalizing symptoms in determining suicide attempt and suicide among adolescents and young adults aged 12–26 years.
- Only longitudinal studies were included, ensuring that exposure to the factors assessed preceded the outcome.
- There is a significant association between all symptoms, mainly in relation to internalizing symptomatology, specifically in depressive symptomatology, and in externalizing symptomatology and suicide attempt in youth and young adults.

Limitations

- Heterogeneity was severe for all types of symptoms and suicide attempts.
- For the Population attributable risk (PAR) estimate, only three of the studies provided data, from a total of five samples.
- More longitudinal studies are needed to better understand the complex relations with internalizing and externalizing symptoms as risk factors for suicidal behavior and suicide among adolescents and young adults.

Introduction

Suicide is a leading cause of death worldwide, and one of the three main causes of death in young people aged <25 years (1–3). Globally, suicide deaths have increased by 60% over the last 45 years, with a higher number of these deaths occurring among adolescents and young adults(4). For these reasons, the European Commission and the WHO encourage

professionals to increase the availability of information on this area, in order to prevent it (5,6).

Risk factors associated with suicidal behavior

There is abundant literature on risk factors associated with suicidal behavior. These include prior presence of suicidal behaviors (7,8); exposure to traumatic stressful events, such as abuse or victimization; the existence of some legal factors (9–13); certain psychological factors, such as hopelessness, impulsiveness, or low self-esteem (14–18); the presence of somatic or disabling problems (19,20); or previous history of mental disorders, especially emotional (depression and anxiety) and behavioral disorders (21,22).

Internalizing and externalizing symptoms as risk factors associated with suicidal behavior.

Mental disorders have been highlighted as some of the strongest predictors of suicidal behavior among adolescents and youth. A recent meta-analysis (21) indicated having an affective disorder (OR = 6.04; 95% CI = 2.7–13.49) as the best predictor of suicide attempts, followed by anxiety disorders (OR = 3.5; 95% CI = 2.49–4.94), although in the latter case, statistical significance was not reached. Regarding behavioral disorders, this study indicates that disruptive disorders (OR = 3.14, 95% CI = 1.69–5.83) were significantly associated with suicidal acts.

In general, the association between suicide and presence of mental disorders is uncertain when we consider the symptoms of emotional disorders. These symptoms would correspond to internalizing and externalizing behaviors and symptoms, following Achenbach, Edelbrock, & Howell's (23) classification, with internalizing symptoms entailing manifestations of anxious, depressive, and somatic problems, and externalizing symptoms including problems related to aggressiveness, inattentiveness, disobedience, and criminal behavior. With regard to symptoms, research focusing on college students has demonstrated a strong association between the middle, lower, and subclinical symptomatic levels of depression and suicidal thoughts/ideation (24–26). The concurrence of symptoms of depression and anxiety disorder is related to more severity (27), characterized by more clinical impairment and a higher risk of suicide attempts(28,29). Similarly, subclinical depression and anxiety are associated with an increased risk of suicide (30). In addition, depression and anxiety rates increase dramatically during adolescence, with a lifetime prevalence of 12.60% for depression and 32.40% for anxiety disorders (31).

Another meta-analytic review (32) of the associations between potential risk factors for suicide according to the domains of the Research domain Criteria (RDoC) five in the Negative Valence Systems category, included variables that correspond to those in our meta-analysis (depressive mood, guilt, hopelessness, agitation, aggression, nervousness, neuroticism, perfectionism, Strained, tense, tension, pessimism, hostility, anger at society, negative attribution, brooding, sanguinity, reflective pondering, dysphoria, rumination, irritability, reflection, unhappiness, compulsiveness, panic attack, and negative temperament). Most of the risk factors were classified under the domain of the Negative Valence System (n = 173). Negative Valence Systems category "… was also significantly related to suicidal ideation (Adjusted OR; wOR) = 1.72 95% CI; 1.54–1.93), attempted suicide (wOR = 1.31 95% CI; 1.20–1.43), and suicide deaths (wOR = 1.47 95% CI; 1.26–1.70). However, although Glenn et al., (32) include many predictors, they also include populations of any age and do not exclude studies with non-longitudinal designs.

Based on the above, the present study set out to conduct a meta-analysis of literature, with the objective of estimating the role of internalizing and externalizing symptoms in determining suicide attempt and suicide among adolescents and young adults aged 12–26 years, using meta-analysis.

Aims of the study

We assessed (i) the risk of suicide attempts and of suicide deaths in youths and young adults with internalizing and externalizing symptoms; and (ii) the population attributable risks of suicide attempt and suicide associated with externalizing symptoms. Based on previous published meta-analyses, we hypothesized that youths and young adults with internalizing or externalizing symptoms have higher rates of suicide attempts and suicide than youths and young adults without these symptoms.

Method

Search Strategy

This study stems from a broader systematic review carried out up to January 2017. The search strategy was conducted following the PRISMA recommendations for a systematic review and the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) guide regarding the management and communication of results (33). Documents were selected using MeSH-type descriptors (longitudinal studies, risk, deliberate self-harm, antecedent,

association, suicide, etc.). We searched the databases of the Cochrane Library, Embase, Medline, PsychINFO, and the Web of Science. We searched grey literature using the OpenGrey European database and examined reference lists from previous reviews and books. No restriction for language or year of publication was applied. At least three attempts were made to contact authors of articles written in a language other than English or Spanish. The protocol according to which the review was performed is available at the International Prospective Register of Systematic Reviews, PROSPERO (Reg: CRD42013005775) (34) (more information about the search strategy and selection criteria of the broad systematic review is provided in supplementary document, Text S1, and Table S1 as is the MOOSE checklist).

Eligibility Criteria

Initially, a wide-ranging search strategy was carried out. The original literature search was performed so as to identify predictors of suicidal behavior without population or age restrictions. Studies that met eligibility criteria, as follows, were included: (a) reporting suicide attempt or suicide as a dependent variable; (b) assessing at least one risk factor for any of these outcomes; (c) a study population age range of 12–26 years; (d) population-based longitudinal studies (e.g., non-clinical and non-institutionalized sample cohorts, or case controls where the control group was of the same age range as the experimental group and was both non-clinical and non-institutionalized). Studies focusing on institutionalized or clinical samples were excluded to ensure that the results obtained could be generalized to the general population of adolescents. Using a previous expert consensus, the authors decided to use Silverman, Berman, Sanddal, O'Carroll, and Joiner's (35) definitions of suicide (i.e., death by suicide or "any fatal act done with the intent to take one's own life") and attempted suicide (i.e., "any act or self-injury with the intent to die").

The second phase of the review entailed the inclusion of articles assessing only variables related to internalizing symptoms (depressive symptoms, anxiety symptoms, somatic symptoms, and withdrawal) and externalizing symptoms (legal problems, truancy, behavior problems, misleading others, aggression toward others, violence toward others, and behavior problems) with attempted suicide or suicide.

Data Extraction

In order to carry out the review, a multidisciplinary team of psychiatrists, psychologists, statisticians, epidemiologists, and public health professionals was established. Five groups of independent reviewers assessed every reference (total reviewers $10 = 5 \times 2$; each pair of reviewers analyzed 20% of the references). The information contained in supplementary document Text A1 was used for the title review. To minimize selection bias, during the title and abstract reviews, reviewers were blinded to the names of the authors of each article, the journal it was published in, and year of publication. Both the titles and abstracts were peer reviewed.

After a full text review, each reviewer accounted for 20% of the total number of articles included. A form from the Cochrane Collaboration was adapted to collect the data used in the study. A third reviewer was assigned to assess discrepancies between reviewers at the abstract and full-text stage. In the present study, the information collected on internalizing and externalizing symptoms was as follows: for categorical variables, ORs, confidence intervals of 95%, and *p*-values. For continuous variables, the effect sizes or "ES" with a CI of 95% were collected.

Quality Assessment

In order to assess the quality of the studies, the Newcastle-Ottawa scale (NOS) was used (36). This assessment was performed in order to avoid including biased or methodologically deficient studies that could also bias the results of the present review, due to an overall estimate of effect.

Using a "star system," the quality of studies was assessed according to the selection of study groups, the comparability of groups, and the verification of exposure or outcome of interest for case-control or cohort studies, respectively. The highest possible NOS score is nine stars. The quality of the identified studies was assessed by one reviewer, and another reviewer checked each item in the article.

Data Analyses

In the present study, different analyses were performed according to the method used to measure internalizing and externalizing symptoms, either as a categorical or continuous variable. STATA version 13 software was used to perform these meta-analyses. The ES and

standard error (SE) were calculated based on means and standard deviations, using the DerSimonian-Laird (DL) model. Multivariate analyses prevailed over the bivariate analyses. Stratified analyses were also taken into account, wherever possible. In the event that the article did not provide sufficient data to perform the meta-analysis, a maximum of three e-mails were sent to the authors to collect this information.

The heterogeneity assessment was performed using the chi-square test, the Higgins test (I^2) (37), and the Galbraith graph. Significance was assumed when the p-value of a chi-square test was $<.10$, and using the I^2 estimator, heterogeneity was defined as low ($<30\%$), moderate ($30\%-50\%$), and severe ($>50\%$) (37). A random effects model was used to perform the meta-analysis, as we assumed that some differences would occur in the studies.

Publication bias was determined using funnel plots and Egger's regression asymmetry test (39). In all the tests, the presence of significance must be understood as publication bias. In the presence of significant asymmetry, we used the Duval and Tweedie Trim and Fill test (40) to reduce the impact of publication bias by imputing possible unpublished studies, and obtaining a new pooled estimate.

Finally, sensitivity analysis was performed taking into account those variables that a priori could be a source of heterogeneity between studies. The variables were: (1) study design: cases and controls; (2) low quality of included studies: <6; (3) outcome studied (suicide or attempted suicide); (4) instruments used to measure internalizing/externalizing symptomatology; and (5) abnormal OR or ES values. Population attributable risk (PAR) was also calculated from cohort studies using this formula:

$$\text{PAR} = \frac{P(RR-1)}{1+P(RR-1)}$$

where P is the prevalence of risk factors (internalizing or externalizing symptoms) obtained through data from some of the cohort studies included in the meta-analysis, and RR is the relative risk of suicide attempt with internalizing or externalizing symptoms, based on data from the cohort studies included. To convert the OR to relative risk, the following formula was used:

$$\text{RR} = \frac{OR}{(1-P_0)+P_0 OR}$$

where OR is the odds ratio of suicide attempt with any internalizing or externalizing symptoms versus no presence of internalizing or externalizing symptoms, and P_0 is the prevalence of suicide attempts in adolescents and youth, without internalizing or externalizing symptoms, calculated through meta-analysis using data from four of the included articles.

For meta-analyses, we assessed all variables for internalizing/externalizing symptoms as categorical variables with one meta-analysis, then all continuous variables in another meta-analysis. Lastly, depending on the amount of data obtained from the studies, different meta-analyses were performed with different variables of internalizing symptoms, and separately with different variables of externalizing symptoms.

Results

Selection and inclusion of studies

The database search revealed a total of 26883 articles, once the duplicates were eliminated. A total of 1701 references were screened, of which, after applying the exclusion criteria, 1480 were excluded; the reasons are detailed in Figure 1. Finally, 41 studies evaluating internalizing or externalizing symptoms were included in the qualitative synthesis, with a total of 283505 participants. A total of 18 studies were excluded as they lacked the data needed to perform the meta-analysis and 24 were included in the meta-analysis, with a total of 217550 participants.

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Characteristics of included studies

Table 1 shows the characteristics of the included studies. In terms of study design, it can be seen that more than half are cohort studies (51.21 %). Of these, most of the samples were from the United States (45.00 %); only one study did not report the recruitment site of the participants (41). In addition, suicide attempt was the outcome studied in 87.80% of the articles; only 5 assessed the risk of death by suicide (12.19%).

On the one hand the percentage of articles that included some internalizing symptom was 78.04%; 84.37% of which evaluated depression symptoms; 21.87%, anxiety symptoms; 12.50%, somatic symptoms; 6.20%, withdrawal; and 12.50% evaluated internalizing

symptoms as a general factor. On the other hand, 51% evaluated externalizing symptoms: 47.62% assessed crime or legal problems; 19.05%, violence on others; 13.70%, assault on others; 28.57%, truancy; and 23.81%, externalizing symptoms in general.

Concerning the measures employed, it should be noted that most of the studies used the Beck Depression Inventory (BDI) (42), the Center for Epidemiological Studies-Depression Scale (CES-D) (43), and the Youth Self Report (YSR) (44), which all had equal percentages (9.75%). With regard to the assessment of externalizing symptoms, 29.71% of the studies had used a non-validated instrument.

----------------------------------Table 1--

Quality assessment of studies

More than half of the studies (56%) obtained ≥6 stars. All cohort studies, with the exception of Salzinger et al.'s (45), obtained a star for the representativeness of the exposed (subjects with internalizing or externalizing symptomatology) and unexposed (subjects without internalizing or externalizing symptomatology) cohort, which suggests that exposed and unexposed youths represented the population study.

However, only three studies reported verification of results through measures such as interviews with blind professionals or measures other than self-reporting (see online supporting information Table S2).

Data Synthesis

Overall, data from 26 (66.66%) studies were used to perform the different meta-analyses; 33.33% of 26 studies presented adjusted data and in 45.83% of the studies, the data had been obtained from multivariate analyses. Of the 26 included studies, we used the data obtained from 72 samples to carry out the meta-analyses. On the one hand, the analysis of general internalizing symptoms measured as a continuous variable was carried out with 29 samples of these 72. Of the 29 samples, 8 were used to analyze anxiety symptoms and 19 were used to examine depressive symptoms. On the other hand, in the analysis of the internalizing symptoms measured as a categorical variable, only 8 samples of the 72 included were used, which evaluated depression symptoms. Finally, in the analysis of general externalizing symptoms, 8 samples measured the symptoms as continuous variables and 21, as categorical

variables. Of these 21, 12 samples could be used to specifically analyze the variables related to legal problems.

General internalizing symptoms Most studies (87.50%) showed a significant association between internalizing symptoms and future suicide attempts or completed suicide. For internalizing symptoms measured as continuous variables, total ES with all 29 samples showed a large effect of 0.93 (0.67 to 1.18). According to the outcomes of data synthesis, we identified substantial heterogeneity ($I^2 = 92\%$); the Galbraith graph also represented this heterogeneity, in which, although a large part of the studies were located in the central zone, 9 samples were outside the lines (46–50) and were the ones causing the heterogeneity. However, according to Egger's test, publication bias was not significant ($p = .41$) and heterogeneity did not become significant in the sensitivity analysis phases. The distribution of the samples is shown in Figure 2.

-------------------------- Figure 2--

Internalizing symptoms: depressive symptoms. As for the values for depressive symptoms, a significant association between having symptoms of depression and attempted or completed suicide was reflected in 66.66% of studies. On the one hand, for the variable assessed as a categorical variable, the total OR value, with 8 samples, was OR = 6.57 (95% CI 4.72 to 9.17). Heterogeneity was moderate and not significant, with a value of $I^2 = 46.30\%$; this is reflected in the Galbraith graph, where all studies are grouped between the lines. Publication bias was almost not significant, with a value of $p = .386$.

In the case of depressive symptoms evaluated as a continuous variable, the total ES value, with 19 samples, was large: 1.00 (0.65 to 1.37). Heterogeneity of the studies was severe and significant ($I^2 = 93.40\%$); however, publication bias was not significant ($p = .29$). In addition, Galbraith's graph reflects this heterogeneity and shows that, once again, the studies by Miranda et al., Stein et al., and Wichstrom and Rossow (47–49) were outside the lines. In both cases, wherein symptoms of depression were evaluated as categorical and continuous variables, after sensitivity analyses, the value of heterogeneity did not decrease and the results with a higher ES and a more significant ES were found by including all the articles in the analysis. The distribution of the studies can be seen in Figure 3.

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Internalizing Symptoms: Anxiety Symptoms. Of the studies that provided the eight samples for the meta-analysis, 66.66% indicated a significant relationship between having a certain anxiety symptom and attempted suicide or consummated suicide. The overall ES was moderate, with a value of 0.65 (0.12 to 1.19). In this case, like the rest of the meta-analysis, repeated severe heterogeneity ($I^2 = 91.01\%$) and non-significant publication bias ($p = .917$) were noted among these studies. Again, studies by Miranda et al. (47) and Stein et al. (48) were outside the lines in Galbraith's graph. Finally, no samples were excluded as, after sensitivity analyses, the value of heterogeneity did not decrease until it was not significant. The distribution of the samples is shown in Figure 3C.

General Externalizing Symptoms. Most of the studies analyzing externalizing symptoms, at 73.91%, showed a significant association with attempted or completed suicide. Specifically, in the studies that evaluated the externalizing symptoms as continuous variables (8 samples), a moderate effect size was obtained, at 0.76 (0.53 to 0.99), with $I^2 = 62.32\%$; this demonstrated severe and significant heterogeneity. Publication bias was non-significant ($p = .723$).

For studies measuring externalizing symptoms as categorical variables (25 samples), a significant total OR value = 2.86 (95% CI 2.05 to 3.59) was obtained; there was a severe and significant heterogeneity across the studies ($I^2 = 84.20\%$). Publication bias was not significant ($p = .061$). A study by Davidson et al. (46) and some samples from Beautrais et al. (51) had an upper limit of the OR confidence interval greater than 300, and were excluded. In the case of the study by Beutrais et al. (51), we eliminated the sample in which the legal problems of the persons studied were assessed through other informants, and in the case of Davidson et al.' study (46), the sample of cases was quite small (14 persons). After exclusion of these studies, with a total of 21 samples, the results changed minimally; a significant total OR value = 2.59 (95% CI 2.01 to 3.21), and severe and significant heterogeneity among the studies ($I^2 = 84.20\%$) was shown, with non-significant publication bias ($p = .082$).

The final distribution of the samples after exclusion is shown in Figure 4.

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Externalizing symptoms: legal problems. Eighty percent of the studies showed a significant association between legal problems and attempted suicide or suicide. The data obtained from 15 samples allowed us to perform a meta-analysis to check the association between legal problems and attempted suicide or completed suicide. In this case, significance was obtained, with a total OR value of 4.41 (95% CI 2.57–7.78). However, we identified substantial heterogeneity according to the outcomes of data synthesis ($I^2 = 78\%$) and publication bias, with $p = .048$. Again, Davidson et al.'s (46) study and Beautrais et al.'s (51) samples were excluded. After exclusion, we obtained an OR = 3.36 (95% CI 1.99–5.69); heterogeneity remained severe and significant ($I^2 = 77.40\%$), but publication bias decreased to non-significant ($p = .304$).

The distribution of studies after exclusion of some is shown in Figure 4C.

Population attributable risk (par). For the PAR estimate, only the studies that analyzed externalizing symptoms, behavior problems, truancy, police contact, and serious offense provided data. Only three of the studies provided data, from a total of five samples. We estimated the PAR based on the range of prevalence values of being exposed to these externalizing symptoms. The rate of suicide attributable to this factor is 16%, and according to the data, the elimination of externalizing symptoms would theoretically reduce suicide attempts by 40% (see online supporting information Table S3).

Discussion

Summary of main findings

After reviewing all the studies, the results show that adolescents and young adults with internalizing and externalizing symptoms are at a higher risk of suicide attempts and suicide. The greatest significance was found in the association between having symptoms of depression and suicide attempts, although moderate heterogeneity was demonstrated in the different studies included. The ES obtained in the meta-analysis of all internalizing symptoms was large. The magnitude was found to be moderate in the meta-analysis and is also significantly associated with attempted suicide or suicide, which constitute externalizing symptoms. However, this ES is higher when only calculating the values of the variables that measure legal problems. A meta-analysis of anxiety symptoms yielded a lower ES value, with a moderate magnitude.

In all the meta-analyses, although the heterogeneity obtained was high or moderate, it did not decrease after sensitivity analyses. However, according to the information in Table S2, heterogeneity may be attributed to differences between the included population studies (with differences between methodological and contextual factors) and differences in the definitions of risk factors. On the one hand, in the case of the meta-analysis of studies measuring externalizing symptoms as categorical variables, four samples were found to have extreme values at the intervals of the OR (upper limit greater than 300). It was therefore decided to exclude these samples from studies by Davidson et al. (45) and Beautrais et al. (50), to prevent them from producing variations in the meta-analytic values. In relation to Davidson et al.'s (45) study, the abnormal values may be due to the fact that the sample is small, as it included only 14 people who had attempted suicide. On the other hand, in the study by Beautrais et al. (50), abnormal OR values may be due to different ways of collecting information relating to the variables, since the values are normal in the sample that self-reported having had problems related to the law; however, samples in which the legal problems were evaluated by other informants yielded abnormal values. Although having symptoms of depression, lack of discipline, legal problems, and violence towards others are related to death by suicide, evidence pertaining to this is sparse, with only 12.50% of studies evaluating completed suicide as an outcome.

With regard to the calculation of PAR, it should be noted that only five samples could be used. Therefore, although the information obtained is relevant, it is not robust.

Strengths and Limitations

Our meta-analysis has several strengths: (i) to our knowledge, there are no other meta-analyses about suicidal behavior and internalizing and externalizing symptoms in the age group examined in our study; (ii) study selection was conducted without restrictions on language and year of publication, using a peer review process at the selection stage, and independent peer review in data extraction; certain methods were used to minimize bias; (iii) we contacted authors of other studies for more information; (iv) we also searched grey literature; and (v) only longitudinal studies were included, ensuring that exposure to the factors assessed preceded the outcome. From our point of view, this decision makes our findings more relevant to establishing the temporal order of events and minimizes bias.

Some limitations to our study deserve discussion; (i) severe heterogeneity was observed, being attributed to the variety of variables evaluated and the different methods used in the analysis of these variables; (ii) very few studies were identified that evaluated internalizing or externalizing symptoms as a risk factor for death by suicide, which did not allow us to estimate the true magnitude of the effect; (iii) the PAR obtained is not very robust due to the paucity of studies with data available for calculation; and (iv) the NOS scale, designed to assess the quality of longitudinal studies, was used, although evidence for its validity is still limited (52). All these points indicate the urgent need to investigate these risks further.

Comparison with other studies

Our findings are consistent with those of previous studies demonstrating the relationship between internalizing and externalizing symptomatology with suicide attempts and suicide in adolescents and young adults. However, to the best of our knowledge, no previous meta-analysis has considered internalizing and externalizing symptoms, except in relation to disorders. The results obtained in this meta-analysis are consistent with those of Gili et al.'s meta-analysis (21). Gili et al.'s meta-analysis (21) results from the same wide-ranging review as that in this study; however, the inclusion criteria differ, as studies evaluating mental disorders were included and those evaluating symptomatology without mental disorders were excluded. It is interesting that, in our case, although mental disorder was not studied and only symptoms were included, the results proved similar. In Gili et al.'s (21) meta-analysis, the OR value (6.04; 95% CI) in studies involving affective disorders is similar to the value that we obtained in studies involving depression symptoms (OR = 6.58; 95% CI). In addition, the same meta-analysis also found an association between having a disruptive disorder and performing a suicidal act (OR = 3.14; 95%CI), and our results show a similar OR (3.36; 95%CI) in the overall outcome of the studies that included having had some legal problem. On a different note, although different statistics are used in Gili et al.'s (21) meta-analysis (OR) and our study (ES), both studies showed a relationship between having an anxiety disorder or symptom and suicide attempts (OR = 3.5; 95%CI vs. ES = 0.65).

In another meta-review consisting of 6 reports (1995 to 2017) and 2303 participants diagnosed with a mood disorder from the United States and South Korea, depression disorder was one of those reflecting a larger and more significant association with suicide risk in the different studies (53).

Although suicide in early life has a fatal outcome, with huge emotional, social, and physical consequences for family and peers, its etiology and prevention are poorly understood. Our study fills a knowledge gap in the world of research regarding the risk factors associated with suicide attempts in adolescents and young adults. To our knowledge, this is the first meta-analysis to evaluate the association between internalizing and externalizing symptoms and suicide attempts in this population.

Future research and recommendations

The evidence suggests that there is a significant association between, mainly in relation to internalizing symptomatology, specifically in depressive symptomatology, and in externalizing symptomatology and suicide attempt. There is also an association, although to a lesser extent, between anxious symptomatology and legal problems with attempted suicide or suicide. However, these data are not conclusive for the generalization of the rest of the symptoms (i.e., somatic symptoms, school absenteeism, violence towards others, and aggression towards others), since, although they reflected a significant association with suicide attempts in the various articles, they could not be analyzed separately due to the small number of variables. In this sense, more longitudinal studies are needed to evaluate suicide and suicide attempt, as well as death by suicide and the factors involved. Similarly, it would be interesting to have more studies evaluating the incidence of suicidal behavior and to be able to obtain scientific information on each risk factor separately, in order to carry out actions, research and programs focused on each factor.

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TABLE 1. Study characteristics of included articles.

Author (Study)	Country	Outcome	Population	Age Range (years)	Study Design	Length of Follow-up	Total Sample (at baseline in cohort studies) (%women)	Sample at the End of Follow-up (%attrition)	%of Suicide Attemtps or Suicide During the Follow-up	Instrument Used
Davidson et al.(1989) (46)	USA	S	Students	14-19	Case-Control	*a*	14 cases vs. 39 controls (10.8)	*a*	*a*	*a*
King et al. (1990)(54)	USA	SA	Females	13 - 16	Case-Control	*a*	19 cases vs. 21 controls (100)	*a*	*a*	The short version of the Personality Inventory for Children (PIC) (55)
Rotheram-Borus et al.(1990) (56)	USA	SA	Students	12–17	Case-Control	*a*	77 cases vs. 23 controls	*a*	*a*	Beck Depression Inventory (BDI)(42)
Goldney et al.(1991)(57)	Australia	SA	Students	18-25	Cohort	8 years	1014 (51.7)	472 (53.45)	2.54	The measure of pessimism: the hopelessness scale (58)
Garnefsky et al.(1992)(59)	Netherlands	SA	Students	15-16	Case-Control	*a*	285 cases vs. 285 controls (64.9)	*a*	*a*	Monitoring the Future Questionnaire (60)
De Wilde et al. (1992;1993)(61,62)	Netherlands	SA	Students	14 - 21	Case-Control	*a*	48 cases (85.4) and 43 (72.1) controls	*a*	*a*	The life event time schedule, Dutch version of State Trait Anxiety Inventory (STAI) (63,64)
Lewinsohn et al.(1994)(65)	USA	SA	Students	14-18	Cohort	1 year	1710 (54)	1508 (11.81)	1.7	Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) (66)
Fergusson and Lynskey (1995)(67)	New Zealand	SA	General	14-16	Cohort	16 years	1265	954 (24.58)	3.0	Self-Report Early Delinquency Scale (68)
Reifman and Windle (1995)(69)	USA	SA	Students	*a*	Cohort	*a*	1360	981 (27.86)	*a*	CES-D (43)

TABLE 1. (continued)

Author (Study)	Country	Outcome	Population	Age Range (years)	Study Design	Length of Follow-up	Total Sample (at baseline in cohort studies) (%women)	Sample at the End of Follow-up (%attrition)	%of Suicide Attemtps or Suicide During the Follow-up	Instrument Used
Beautrais et al.(1997) (51)	New Zealand	SA	General	19.4-21.4	Case-Control	*a*	129 (52.5) cases and 153 (49.7) controls	*a*	*a*	*a*
Stein et al.(1998)(48)	Israel	SA	General	12 - 28	Case-Control	*a*	51 cases vs. 194 controls	*a*	*a*	BDI, STAI and Suicidal Potential Scale (SPS) (42, 64, 70)
Brent et al.(1993; 1999)(10,71)	USA	S	General	13-19	Case-Control	*a*	140 cases vs. 131 controls (41.5)	*a*	*a*	YSR (44)
Fergusson et al. (2000) (72)	New Zealand	SA	General	14-16	Cohort	16 years	1063 (49.8)	881 (17.1)	*a*	CIDI(73)
Grøholt et al.(2000) (74)	Norway	SA	Students	13-19	Case-Control	*a*	232 cases: 91 HAS (90) and 141 SRSH (77) and controls 1736 (52)	*a*	*a*	Depressive Mood Inventory (DMI) (75)
Lyon et al.(2000)(76)	USA	SA	African American	12–17	Case-Control	*a*	38 cases vs. 76 controls (82)	*a*	*a*	The Psychiatric Consultation Checklist (77)
Borowsky et al.(2001)(78)	USA	SA	Students	*a*	Cohort	1 year	20745	*a*	3.6	*a*
Çetin et al.(2001)(79)	Turkey	SA	General	14 - 20	Case-Control	*a*	33 cases (69.7) vs. 50 controls (52)	*a*	*a*	BDI , Symptom Checklist 90 (SCL-90) (42,80)
Wichstrom and Rossow (2002)(49)	Norway	SA	Students	12 -22	Cohort	2 years	9679 (50.9)	7637 (21.09)	1.74	DMI (75)
Bearman and Moody (2004) (81)	USA	SA	Students	*a*	Cohort	1 year	20745 (50)	13465 (35)	4	ítem: No. Of physical fights in past year
Ialongo et al.(2004) (82)	USA	SA	African Americans	19 - 20	Cohort	11 years	1197 (56)	747 (38)	4.2	Baltimore How I Feel-Youth Report (BHIF-YR), Teacher Observation of Classroom Adaptation-Revised (TOCA-R)(83,84)
Donald et al. (2006) (85)	Australia	SA	General	18-24	Case-Control	*a*	95 cases 380 controls (48)	*a*	*a*	CES-D (43)
Rodriguez-Cano et al. (2006) (86)	Spain	SA	Students	13-15	Cohort	2 years	1766 (50.2)	1076 (39)	3.8	*a*

TABLE 1. (continued)

Author (Study)	Country	Outcome	Population	Age Range (years)	Study Design	Length of Follow-up	Total Sample (at baseline in cohort studies) (%women)	Sample at the End of Follow-up (%attrition)	%of Suicide Attemtps or Suicide During the Follow-up	Instrument Used
Salzinger et al. (2007) (45)	USA	SA	Students	15-20	Cohort	6 years	100 abused vs. 100 non-abused (35)	153 (23.50)	12.4	YSR (44)
Thompson et al. (2007)(87)	USA	SA	Students	12–26	Cohort	7 years	18924 (49)	15034 (20.5)	1.2	CES-D (43)
Dupéré et al. (2008)(88)	Canada	SA	General	18-29	Cohort	8 year	3088	2776 (10.10)	*a*	*a*
Goldstein et al. (2008)(89)	USA	S	General	13-19	Case-Control	*a*	140 cases vs. 131 controls (41.5)	*a*	*a*	K-SADS (66)
Larsson and Sund (2008)(90)	Norway	SA	Students	12-18	Cohort	1 year	2397 (49.4)	2370 (0.8)	3.0	YSR (44)
Wong et al. (2008)(91)	China	SA	General	12 -18	Case-Control	1 year	1050 cases vs. 49 controls	*a*	*a*	CES-D, Chinese version of the STAI (43,92)
Peter and Roberts (2010) (93)	Canada	SA	General	15 - 22	Cohort	5 years	2499 (51.1)	2499 (*a*)	45.9	3 ítems for depression symptoms (alpha .73) and 4 ítems for anxiety index (alpha .72)
Roberts et al. (2010) (94)	USA	SA	General	11 - 17	Cohort	1 year	4175 (48.9)	3134 (24.9)	.95	*a*
Christiansen et al. (2012) (95)	Denmark	SA	General	10 - 21	Case-Control	22 years	3718 cases vs. 185900 controls (17.3)	*a*	*a*	*a*
Guan et al. (2012) (41)	*a*	SA	Students	16-17	Cohort	2 years	712	399 (44)	*a*	Mood and feelings

|										questionnaire (MFQ) (96)
Wong et al. (2012) (97)	USA	SA	Students	14-22	Cohort	8 years	6504	*a*	1.3	CES-D (43)
Maraš et al. (2013) (98)	Serbia	SA	General	15-18	Case-Control	*a*	32 cases vs. 30 controls	*a*	*a*	YSR (44)
Mustanski and Liu (2013) (99)	USA	SA	LGBT	17-21	Cohort	1 year	237(52)	212(10)	8	BDI (42)
Mars et al. (2014) (100)	United Kingdom	SA	General	16-17	Cohort	16 years	14062	4799(34.1)	*a*	Short Mood and Feelings Questionnaire (101)
Miranda et al.(2014) (47)	USA	SA	Students	12-26	Cohort	*a*	1729(60)	506 (21)	8	BDI (42)

TABLE 1. (continued)

Author (Study)	Country	Outcome	Population	Age Range (years)	Study Design	Length of Follow-up	Total Sample (at baseline in cohort studies) (%women)	Sample at the End of Follow-up (%attrition)	%of Suicide Attemtps or Suicide During the Follow-up	Instrument Used
Scott et al. (2015) (102)	USA	SA	Students, Girls	14-26	Cohort	8 years	2450(100)	1950(20)	5.3	Child Symptoms Inventories (103)
Zhao and Zang (2015) (50)	China	S	General	15-24	Case-Control	*a*	141 cases vs. 174 controls	*a*	*a*	The Hamilton Depression Rating Scale (HAM-D) (104)

Note: a = Not applicable; USA = United States; HAS=Hospitalized Attempted Suicide; SA = Suicide attempt; S = Suicide; SRSH=Self-Reported Attempted Suicide

PRISMA 2009 Flow Diagram
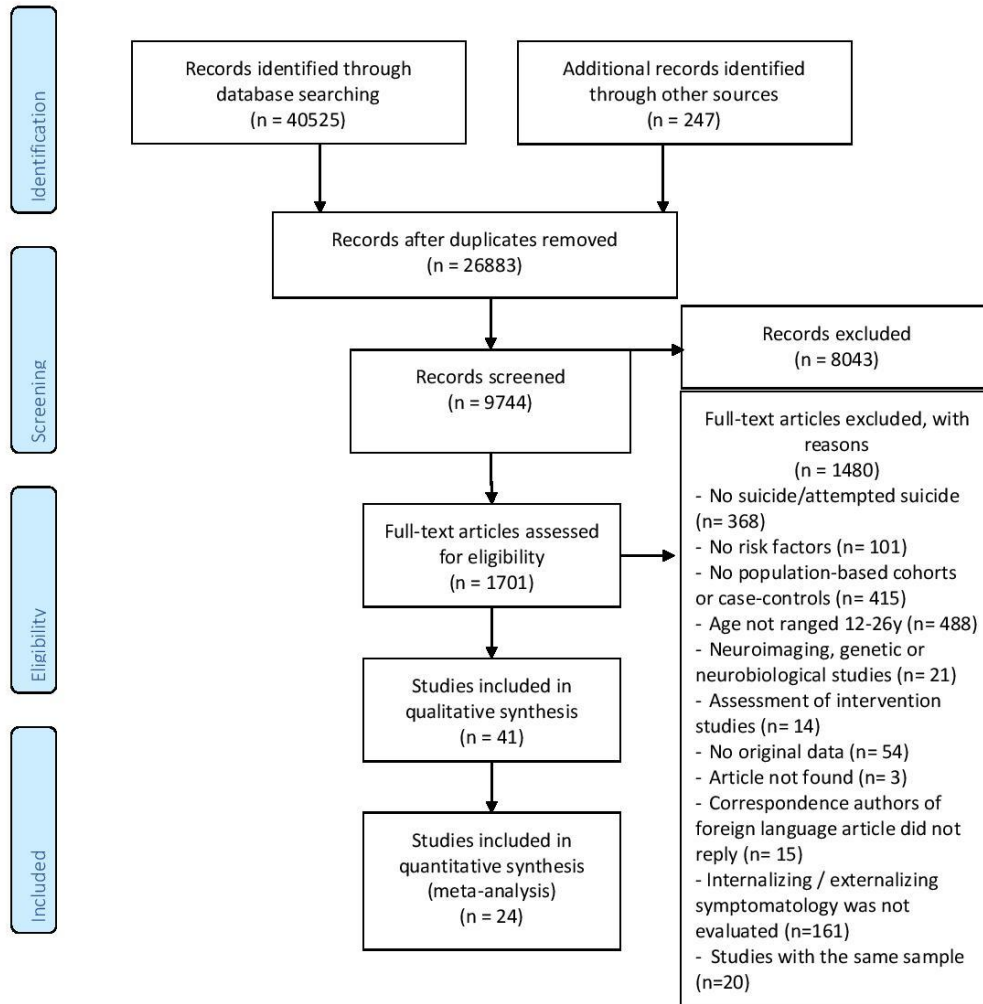
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses:*
The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Fig. 1. Modified version of PRISMA diagram of included studies.

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