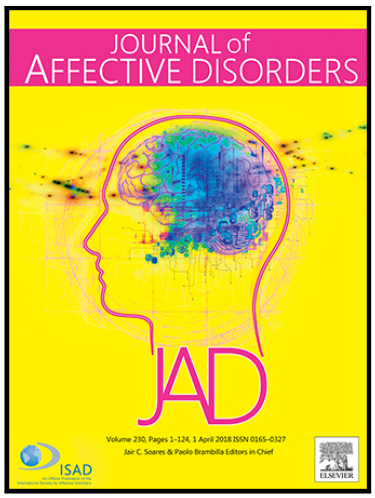

Mental disorders as risk factors for suicidal behavior in young people: a meta-analysis and systematic review of longitudinal studies

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Highlights

- This is the first systematic review and meta-analysis based on longitudinal studies analysing mental disorders and psychiatric comorbidity on suicidal behaviour among young people.
- Mental disorders increase the risk for suicide attempts in young people.
- In particular affective disorders predicted suicide attempts in young people.
- Mental disorders and comorbidity are strong predictors of suicide behavior.

Mental disorders as risk factors for suicidal behavior in young people: a meta-analysis and systematic review of longitudinal studies

Running title: Mental disorders and youth suicidal behavior

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ABSTRACT

Background. Suicide is the second leading cause of death for young people. Objective: To assess mental disorders as risk factors for suicidal behaviour among adolescents and young adults including population-based longitudinal studies.

Method. We conducted a systematic literature review. Bibliographic searches undertaken in five international databases and grey literature sources until January 2017 yielded a total of 26,883 potential papers. 1,701 full-text articles were assessed for eligibility of which 1,677 were excluded because they did not meet our eligibility criteria. Separate meta-analyses were conducted for each outcome (suicide death and suicide attempts). Odds ratio (OR) and 95% confidence intervals (95%CI) and beta coefficients and standard errors were calculated.

Results. 24 studies were finally included involving 25,354 participants (12-26 years). The presence of any mental disorder was associated with higher risk of suicide death (OR=10.83, 95%CI=4.69-25.00) and suicide attempt (OR=3.56; 95%CI 2.24-5.67). When considering suicidal attempt as the outcome, only affective disorders (OR=1.54; 95%CI=1.21-1.96) were significant. Finally, the results revealed that psychiatric comorbidity was a primary risk factor for suicide attempts.

Limitations: Data were obtained from studies with heterogeneous diagnostic assessments of mental disorders. Nine case-control studies were included and some data were collected in students, not in general population.

Conclusions. Mental disorders and comorbidity are strong predictors of suicide behaviour in young people. Detection and management of the affective disorders as well as their psychiatric comorbidity could be a crucial strategy to prevent suicidality in this age group.

Key words: suicide, mental disorders, young people

Introduction

In some countries suicide is the main cause of death and globally it is the second cause in the 15-29-year-old people group (World Health Organization, 2016; Lozano et al. 2012) In some geographical areas, suicide rates increase steadily with age while in others there is a peak in young adults rates that subsides in middle age according to recent data from the World Health Organization (2014). In the National Comorbidity Survey, 12.1% of USA adolescents experienced lifetime suicide ideation, 4.0% developed a suicide plan and 4.1% committed suicide attempt (Nock et al, 2013). Similar prevalence rates of suicidal attempts were found in Europe: 4.2% of more than 12.000 European adolescents reported attempting suicide during their lifetime (Carli et al. 2014). Suicidal thoughts and suicidal behaviour also seem to be common among college students (Mortier et al, 2018a; Mortier et al. 2018b; Blasco et al, 2018; Nam et al, 2018). The prevalence of suicide ideation and attempts is generally higher for girls in adolescents (Boeninger et al, 2010), although in some studies statistically significant differences were found only in suicide ideation (Kim et al, 2017).

Different studies have reported a strong association between suicidal behaviour and mental disorders in adults (Harris et al. 1997; Bolton et al. 2008; Nock et al. 2008; Yaldizli et al. 2010; Chesney et al. 2014). However, there is less evidence-based information about the role of mental disorders in young suicidal behaviour despite epidemiological studies showing that 75% of severe mental disorders start before the age of 24 (Kessler et al. 2005; de Girolamo et al. 2012). A large number of studies on mental disorders and suicide do not analyse specific age groups, are based on clinical samples or use a cross-sectional design (Cavanagh et al. 2003; Arsenault-Lapierre et al. 2004; Conner et al. 2007; Cougle et al. 2009; Schneider et al. 2009; Li et al. 2011). Only a small number of longitudinal studies showed that the association between mental disorders and suicide may differ across different ages (Brent et al. 1993; Rowan, 2001; Jeon et al. 2010; Qin, 2011; Park et al. 2014).

Mood disorder and substance abuse appear as a main predictor of suicide behaviour in youths (Carter et a. 2003; Nrugham et al. 2008a; Roberts et al. 2010; Mars et al. 2014a) along with anxiety disorders (Boden et al.2007; Mars et al. 2014b), sleep disturbances (Goldstein et al. 2008), posttraumatic stress disorder (Wilcox et al. 2009), schizophrenia (Hunt et al. 2010) or eating disorders (Beautraris et al. 1998). Personality disorders (impulsive and avoidant-dependent) were more common in adolescent suicide victims than in community samples (Brent et al. 1994). Comparative studies show that psychiatric disorders at the time of death are more frequent among adolescent suicide victims than among community samples (Carter et al. 2003). A case-control psychological autopsy study of people aged less than 20 years old who committed suicide identified mood disorder alone or in combination with conduct disorder and/or substance abuse as a clear risk factor in teenagers (Schaffer, 1996).

Young people with serious suicide attempts also showed high rates of psychiatric comorbidity (54%): affective disorders and substance abuse disorders were the most prevalent comorbid conditions (Beautrais et al. 1998; Kim and Burlaka, 2018). Most of the adolescents with suicidal behaviour assessed in the National Comorbidity Survey meet lifetime criteria for at least one mental disorder (Nock, 2013). Young age at suicide was associated with comorbidity, particularly with personality disorders of cluster B and substance abuse (McGirr et al, 2008; Kim et al, 2003).

Our review has excluded cross-sectional studies and only included longitudinal studies (either prospective cohorts or case–control studies), thus ensuring that exposure to the factors assessed preceded the outcome. Such a decision makes our findings more relevant for establishing the temporal order of events, as well as minimizing bias improving the quality of included data and allowing us to establish valid and robust conclusions (Garg, et al., 2008; Tooth et al., 2005.)

To the best of our knowledge, no systematic reviews have been published assessing mental disorder as risk factors for suicidal behaviour in youth and young adults. The aim of our systematic review and meta-analysis is to investigate three major questions in population-based longitudinal studies: a) the association between mental disorders and suicidal behaviour in young people; b) the presence of psychiatric comorbidity in these suicidal behaviours; c) the specific mental disorders associated with suicidal behaviours in this age-related population. We hypothesized that young individuals with any mental disorder would have higher rates of suicide attempts and suicide completions than their counterparts without mental disease. We also hypothesized that psychiatric disorders comorbidity would increase the risk of suicidality in this age group.

Methods

Search strategy and data sources

This study was conducted using a broader systematic review to identify a comprehensive list of risk factor for suicidal behaviours in ages 12 to 26 years. The original research protocol was registered at PROSPERO International Prospective Register of Systematic Reviews (Alonso et al. 2013). It was also conducted in line with the MOOSE guidelines for systematic reviews (see MOOSE checklist at supplementary material Table S1).

Electronic databases, including the Cochrane Library, Embase, Medline, PsychINFO and Web of Science were systemically searched for potential records until January 31st 2017. In addition, a search of grey literature was conducted using the OpenGrey database. A broad-scope and inclusive initial search strategy was carried out with no restrictions in population or age, in order to identify predictors of suicide-related behaviour. All the search queries and keywords used are provided in Table S2.

Inclusion and exclusion criteria

The inclusion criteria for the studies in the broad-scope review were as follows: (a) studies reporting suicide attempt or suicide as dependent variable defined as any fatal act done with the intention of taking one's own life or any act of self-injury with intention to die; (b) studies assessing at least one risk factor of any of these outcomes (neuroimaging, genetic, and neurobiological studies were excluded); (c) study population age range from 12 to 26 years old; (d) population-based longitudinal studies (non-clinical and non-institutionalized sample cohorts; or case-control where control group was both non-clinical and non-institutionalized population of the same age range). The following exclusion criteria were considered: (a) studies that focused on clinical or institutionalized samples; (b) other suicide-related behaviours (e.g., suicide ideation).

Using the listed criteria, 222 studies were identified for qualitative synthesis from the broader review. To these studies, we then applied the following specific selection criteria for this systematic review: (a) mental disorders using international diagnostic criteria (International Classification of Diseases-ICD or Diagnostic and Statistical Manual of mental disorders-DSM criteria) as risk factors for suicide attempts or suicide and (b) mental disorders assessed using structured or semistructured validated diagnostic instruments.

Data extraction and Quality Assessment

Five groups of two independent peer reviewers used a standardized data form to extract data and performed quality assessments. Discrepancies arising during abstract and full text review were discussed and agreement reached by adjudication of a third author. During the title and abstract review phases, reviewers were blinded from seeing the article's author, journal or year of publication to minimize selection bias.

Relevant data was extracted using a coding manual. We adapted a Cochrane Collaboration data collection form for this review. An independent reviewer examined all data entered in the data collection form. In case of initial discrepancies, consensus among reviewers was required.

The following data were collected from each selected study: (a) sample size; (b) age range; (c) mean age; (d) country of recruitment; (e) study design; (f) suicide outcome (for longitudinal studies, the last measurement point was selected); (g) type of sample recruited; (h) mental disorder; (i) percentage of people exposed to any mental disorder; (j) variables included in multivariate analyses. From cohort studies, additional data was extracted relating to the follow-up: (a) length of follow-up; (b) attrition rates; (c) percentage of suicide attempts; (d) percentage of suicide deaths. Information obtained about risk factors was odds ratio (OR) and the 95% confidence intervals (95%CI), or beta coefficients (β) and standard error (S.E.). Multivariate analysis prevailed over bivariate analysis as it allowed us to control the dependence between single effect sizes from same studies.

Quality of studies reviewed

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of nonrandomized studies (Wells et al., 2014). The NOS is based on a "star system" in which each study is scored on three broad domains: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies respectively. The scale consists of eight items with a 4-point scale of response. A maximum

level of methodological quality is proven with a score of nine stars. The quality of identified studies was assessed by one reviewer who checked each item for each article.

Data analysis

Separate meta-analyses were conducted for the study outcomes (suicidal attempts and suicidal acts). All the different effect size estimates (OR, β) were converted into the same metric (Cohen's *d*). First of all, we calculated the single adjusted effect sizes from each study with a 95% confidence interval (95%CI). Afterward, overall effect sizes were calculated by means of the DerSimonian-Laird approach based on random-effect models (Kelley and Kelley, 2012). Forest plots were provided to make a wider impression of single effect size distribution. For those calculations, we focused on determining whether the presence of at least one mental disorder might influence committing a suicidal attempt or suicide death. A 95% confidence interval and the contrast test based on the *Z statistic* were also given in order to ensure that overall effect sizes were significantly different from zero.

Heterogeneity among studies' effect size was analysed by means of the Cochran's *Q statistic* and the Higgins and Thompson I^2 statistic (Higgins et al. 2003). If Q reaches a *p* value lower than .05, significant heterogeneity among studies is assumed; moreover, heterogeneity can be interpreted taking into account the I^2 statistic (Higgins et al. 2002): low heterogeneity (I^2<30%), moderate (I^2 between 30%-50%) or severe (I^2>50%).

Publication bias was studied by means of Egger's regression asymmetry test. In order to avoid influence of small-study effects the test is based on the arcsine difference (Rücker et al. 2008). Thus, if the t-based test for asymmetry in the funnel plot was not significant, publication bias would be discarded.

In order to test for differences between having been diagnosed with one or more mental disorders and having been diagnosed with each of the studied disorders, we conducted two independent multivariate meta-analyses for suicidal attempts as well as for suicidal acts, assuming the absence of correlations between the effect sizes of the categories. Multivariate meta-analysis allows one to address dependency among effect sizes from the same sample (Berkey et al. 1998; Schwarzer et al. 2014). The method of moments was used as estimation approach.

Simple meta-regression was used to study the influence of methodological quality of primary studies, considering the score in the NOQAS scale as explanatory factor for suicidal attempt and suicidal act independently. Model estimations were extracted by using maximum likelihood-based methods. Rx64 3.0.1 (Packages Meta and Mvmeta) was used to conduct all the statistical and graphical analyses.

Results

The search strategy identified 26,883papers for potential inclusion. After screening titles and abstracts, we reviewed the full text of 1701 potentially eligible articles and excluded 1677. Thr reasons for exclusion are detailed in Figure 1.

After exclusion, a total of 24 studies were included, involving 25,354 participants (aged 12-26 years), mostly based on samples of the general population or students, except one based on lesbian, gay, bisexual youths and another two based on only women. The studies were undertaken in 8 countries: 11 from United States, 5 from New Zealand, 3 from Norway, and 1 from Australia, Brazil, Canada, Finland and United Kingdom. Four of the studies assessed suicide (16.67%), nineteen assessed suicide attempts (79.17%) and only one assessed both suicidal behaviours (4.16%). Ten (41.67%) of the analysed articles used case-control studies and fourteen (58.33%) used a cohort design. Exposure to any affective disorder as a risk factor of suicide and suicide attempt was reported in most of the articles (*n* = 17), followed by substance use/dependence disorder (*n* = 11), personality disorder (*n* = 3), disruptive, impulse-control, conduct disorders (*n* = 5), attention-deficit hyperactivity disorder (ADHD) (*n* = 4), eating disorder (n = 1) and sleep-wake disorder (*n* = 1). Table 1 provides a summary of all studies included (Brent et al. 1993; Carter et al. 2003; Nrugham et al. 2008a; Roberts et al. 2010; Mars et al. 2014b; Boden et al. 2007; Goldstein et al. 2008; Wilcox et al. 2009; Brent et al. 1994; Shaffer, 1996; Fergusson and Lynskey,1995; Reinherz et al. 1995; Beautraris et al.1996; Fergusson et al. 2003; Brent et al.1999; Fergusson et al. 2005; Nock et al. 2007; Brezo et al. 2007; Nrugham et al. 2008b; Hurtig et al. 2012; Mustanski and Liu 2013; Swanson et al. 2014; Nrugham et al. 2015; Caye et al., 2016; Meza et al., 2016).

Figures 2 and 3 depict the distribution of single effects sizes when the presence of any mental disorder is considered as a factor for committing a suicidal act or attempt. Regarding the suicidal act as outcome, four studies were included in the analyses with single *OR* between 5.41 to 41.76 and within-study variance *w* between 12.34% and 34.08%. Brezo et al. (2007) was not included for analysis as it did not specify mental disorder diagnosis. Overall effect size calculated assuming random-effects models was *OR*=10.83 (CI95=4.69, 25.00), being significantly different from zero, *Z*=5.58, p<.01. Heterogeneity among study effect sizes was confirmed as severe, according to *Q* (3)=9.99, *p*<.05; and I^2=70% (CI95=13.70, 89.60). Finally, publication bias was discarded for that outcome, *t* (2)=2.92, p>.05.

Regarding the risk of committing a suicidal attempt studies' single OR were ranged between .50 to 35.32 with a variance *w*=3.80%-6.10%. The estimated overall effect size for that outcome was *OR*=3.56 (CI95=2.24, 5.67), which was significantly different from zero, *Z*=5.35, *p*<.01. That overall effect size was calculated using a sample of 20 studies. Tests for homogeneity stated a severe heterogeneity among single effect sizes, *Q*(19)=447.36, *p*<.01; I^2= 95.80% (CI95=94.50, 96.70). Finally, publication bias was discarded because the test for funnel plot asymmetry was not significant, *t*(18)=1.83, *p*=.08.

In order to test the cumulative effects of suffering one or more mental disorders, multivariate meta-analysis was used. There were not enough studies to test the aim of the suicidal attempt outcome (*k*>3). Thus, we conducted this analysis based on six single effect sizes. We found significant difference from zero estimating loadings for the category "one disorder", *B*=1.91 (95%CI=1.05, 2.78), *Z*=4.33, p<.01; and for the category, "two or more disorders", *B*=2.18 (CI95=.46, 3.90), *Z*=2.43, *p*<.05. To facilitate understanding of these results, we extracted the overall effect sizes for those categories: for the category "one disorder", *OR*=7.61 (CI95=4.41, 13.13), *Z*=7.28, *p*<.01; for the category "two or more disorders", *OR*=8.92 (CI95=1.74, 45.75), *Z*=2.62, *p*<.01.

A multivariate meta-analysis was only conducted for the suicidal attempts (*k* > 3 containing several single effect sizes) in order to test which category of disorders had the strongest influence. Taking into consideration this outcome, 17 studies were incorporated into the multivariate meta-analysis with a total of 36 single size effects. As a result, we found loadings significantly different from zero for affective disorders (*OR*=1.54, CI95=1.21, 1.96), out of the four categories studied (see Table 2). Differential effects on suicidal attempts were found when an affective disorder was diagnosed. Estimates for the rest of studied diagnostic categories were not significant.

Finally, an absence of significant explanatory effect of the methodological quality of studies was observed according to the results derived from meta-regressions (*p*<.05 for both outcomes).

Discussion

Our results show that mental disorders significantly increase the risk of suicide attempts, and especially of suicide in people from 12 to 26 years old. First, based on random effects models the *OR* for complete suicide was 10.83 and for attempting suicide 3.56. Second, a strong association between mental disorders and suicidal attempts was observed when psychiatric comorbidity was present. Third, suicide attempt risk differed in accordance with the mental disorders diagnose across included studies. When specific mental disorders were studied, only affective disorders predicted suicide attempts. Meta-analysis for specific mental disorder as a risk factor for suicide death was not conducted due to the lack of published studies to estimate overall effect sizes.

These results, focusing on young people studies, are in line with those found in previous meta-analyses or systematic reviews in adult populations (Harris and Barraclough, 1997; Cavanagh et al. 2003; Arsenault-Lapierre et al. 2004). The same risk of suicide (10 times more) of being diagnosed of a least one psychiatric disorder was found in a previous meta-analysis (Arsenault-Lapierre et al. 2004). In a Danish longitudinal study, 38% of male and 57% of female suicides aged less than 35 years old had a recorded previous history of hospitalization due to a mental disease (Qin, 2011). Depressive disorders, particularly recurrent depression, were associated with a higher risk of suicide for both young males and females. Substance use disorder and borderline personality disorder also had a strong influence on young people suicidal behaviour. In general, the risk associated with different disorders decline as people become older. Findings from the Danish study should be addressed under the perspective of severe psychiatric disorders due to the focus on mental disorders that required the admittance to a psychiatric inpatient unit. Deaths by suicide were split almost equally between male and female students,

unlike the predominance of male suicide in the general population (Farrel et al. 2016). In a comprehensive national British study in under 20s the number of suicides rose sharply during the late teens in people aged 18-19 years compared with people younger than 18 years: the week before death, 10% individuals had self-harmed and 27% had expressed suicidal ideas and 43% individuals had no known contact with health-care and social-care services or justice agencies (Rodway et al. 2016).

Comorbidity is the rule rather than the exception in people with mental diseases (Katon et al. 2007; Gili et al. 2010; Gili et al. 2011). Depression is a disorder with high mental and physical illness comorbidity (Gili et al. 2010; Moussavi et al. 2007) Such comorbidity results in a poorer prognosis, increased resource utilization, higher costs, disability and poorer treatment compliance (Scott et al. 2009). Literature suggests additive effects of psychiatric comorbidity in adult suicidal behaviour. Published studies involve mental disorders and personality disorders as well as physical conditions in different patterns of comorbidity with the risk of suicidality (Panagioti et al. 2012; Lin et al. 2014; Pompili et al. 2014; Britton et al. 2015; Kavalidou et al. 2017). In the first population-based prospective longitudinal examination of the impact of anxiety disorders in suicidal acts and suicidal ideation, the presence of any anxiety disorder in combination with a mood disorder was associated with a higher likehood of suicide attempts in comparison with a mood disorder alone (Sareen et al, 2005). In a systematic review, comorbidity was four times higher in suicide reattempts when three or more disorders were diagnosed (Mendez-Bustos et al. 2013). In the National Comorbidity Survey Replication anxiety, mood, impulse-control and substance disorders all significantly predict subsequent suicide attempts in bivariate analyses. These associations decrease in multivariate analyses controlling for comorbidity but remain statistically significant suggesting that effects of comorbidity needs to be taken into consideration in a more specific way. A strong positive association was found, with ORs increasing from 3.7 for any one disorder to 12.1 for three. However the ORs associated with having five or more of disorders do not increase or increase at a decreasing rate, compared with the ORs associated with fewer disorders (Nock et al. 2010). Little is known in young populations. Mood, anxiety, impulse-control and substance use disorders significantly predicted subsequent suicide attempts in young (Nock et al. 2013). In our meta-analysis we only have enough studies to analyse comorbidity and suicidal attempts and not for suicide acts. Substance misuse and specific abuse of alcohol and other drugs is currently a common comorbidity in young people. In the aforementioned study although major depression is among the strongest predictors of suicide ideation, it does not significantly predict suicide plans or attempts among ideators. Suicide plans and attempts are predicted by anxiety, impulse-control and substance use disorders. The authors suggest two possible explanations: 1) some disorders are correlated with suicide attempts because they are comorbid with disorders that are independently associated with suicide attempts. 2) much of the association between mental disorders and suicide attempts is explained by some factor common to most disorders, such as an experience of distress or impairment (Nock et al, 2010).

Depression was the most common mental disorder in those who died from suicide (Szanto et al. 2001; Waern et al. 2003). A history of self-injurious thoughts and behaviours put people at risk for later suicidal thoughts and behaviours according to a meta-analysis of 172 studies including at least one longitudinal analysis predicting suicide ideation, attempts, or death (Ribeiro et al. 2016). In a New Zealand study comparing risk factors for suicide and medically serious nonfatal suicide attempts among young under 25 years of age serious suicide attempters tended to have higher rates of mood disorder. The author suggests two possible explanations for this association. Mood disorders could impair the effectiveness of the attempt or alternatively this result may reflect errors of measurement in the assessment of psychopathology (Beautrais, 2002). High impulsivity and weak coping strategies in young people with alcohol use has been suggested as an increased risk factor for suicidal behaviour (McGirr et al 2008). Rates of suicidal attempts or self-harm has risen in young people (Mars et al. 2014a; Yip et al. 2011). In our review, differential effect sizes of committing a suicidal attempt was found with a diagnosis of affective disorder.

Suicide is a complex behaviour involving individual factors, relationships, social and community factors or access to health care systems. Despite the importance of psychosocial factors, stressors, impulsivity traits, cognitive impairments or social isolation in suicidality, our results highlight the relevant role of experiencing mental disorder in the prediction of suicide behaviour among young people. Moreover, a psychiatric comorbidity constitutes a primary risk factor for suicidality in this population. As a consequence, one of the best strategies for suicide prevention is to optimize the management of mental disease in the youth population with a comorbid diagnosis. Two in three people who died from suicide had mental health care contacts during the year prior to death, most commonly primary and specialty outpatient care. Mental health

contact was significantly associated with female gender and age 25-64-year old group. Specific groups such as youth are significantly less likely to access mental health treatment prior to suicide (Schaffer et al. 2016).

Improving the detection of mental disorders and delivering treatments effectively in primary care is crucial to reducing suicide rates in young population combining strategies that have been shown to be effective in other areas of public health (Bauer et al. 2014). In this age group, monitoring psychiatric diseases with new technologies may be an option for a changing pattern of suicide prevention research (Christensen et al. 2016). Comprehensive, multifaceted suicide prevention programs, including gatekeeper training, education and mental health awareness programs, screening activities and programs for suicide survivors were recently associated with a reduction in youth suicide attempt rates (Godoy et al. 2015). School-based suicide prevention programs analysed through randomized controlled trials seems to be effective (Wasserman et al. 2015). A final important issue is to take into account the importance of considering a developmental perspective due to the fact that psychological, behavioural and personal history variables are not static and change in direction and magnitude during the transition into young adults (Thompson et al, 2018). To concentrate all efforts solely in mental disorders would be insufficient (Haw and Hawton, 2015), but their effective detection and short and long-term management of different mental disorders when comorbidity appears is a crucial component to include in the suicide prevention strategies amongst young populations (Turecki and Brent, 2016).

Implications of the study

Our findings strongly support the view that mental disorder is an important risk factor for suicide behaviours in young people. The robust association requires seriously considering an active detection of mental disorders and implies that prevention of suicidal deaths or suicidal attempts should target young people with mood disorders or anxiety disorders and especially those with both conditions in combination with the different patterns of drugs use. Untreated comorbid mental disorders might be missed opportunities to prevent suicidality or at least to avoid the progression from suicide ideation to suicide attempts. Improved services and access to young mental health services could be relevant for reducing suicidality in this age-population group.

Strengths and Limitations

Our review has several strengths. First, this is the first systematic review and meta-analysis based on longitudinal and population-based studies analysing the influence of experiencing a mental disorder and psychiatric comorbidity on suicidal behaviour among young people. Second, our systematic review only included longitudinal studies, ensuring that exposure to the factors assessed preceded the suicide behaviour. In our work, there are several limitations to be mentioned: the data were obtained from studies with heterogeneous diagnostic assessments of mental disorders (DISC, CIDI, SCID, SADS) or just using DSM diagnostic criteria although all these instruments have good psychometric properties; the definition of "suicide attempt" in a context of suicidal behaviour is controversial because it includes deliberate self-harm carried out without suicidal intention;, nine of the articles were case-control studies and some data were collected only in students, not in general population. Finally, longitudinal studies may present shortcomings in establishing temporality between mental disorders and suicidal behaviour e.g. from loss to follow up, measurement of disorder onset, and the focus of the analysis on the last ‘event’ as the outcome.

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Figure 1. PRISMA Flow Diagram

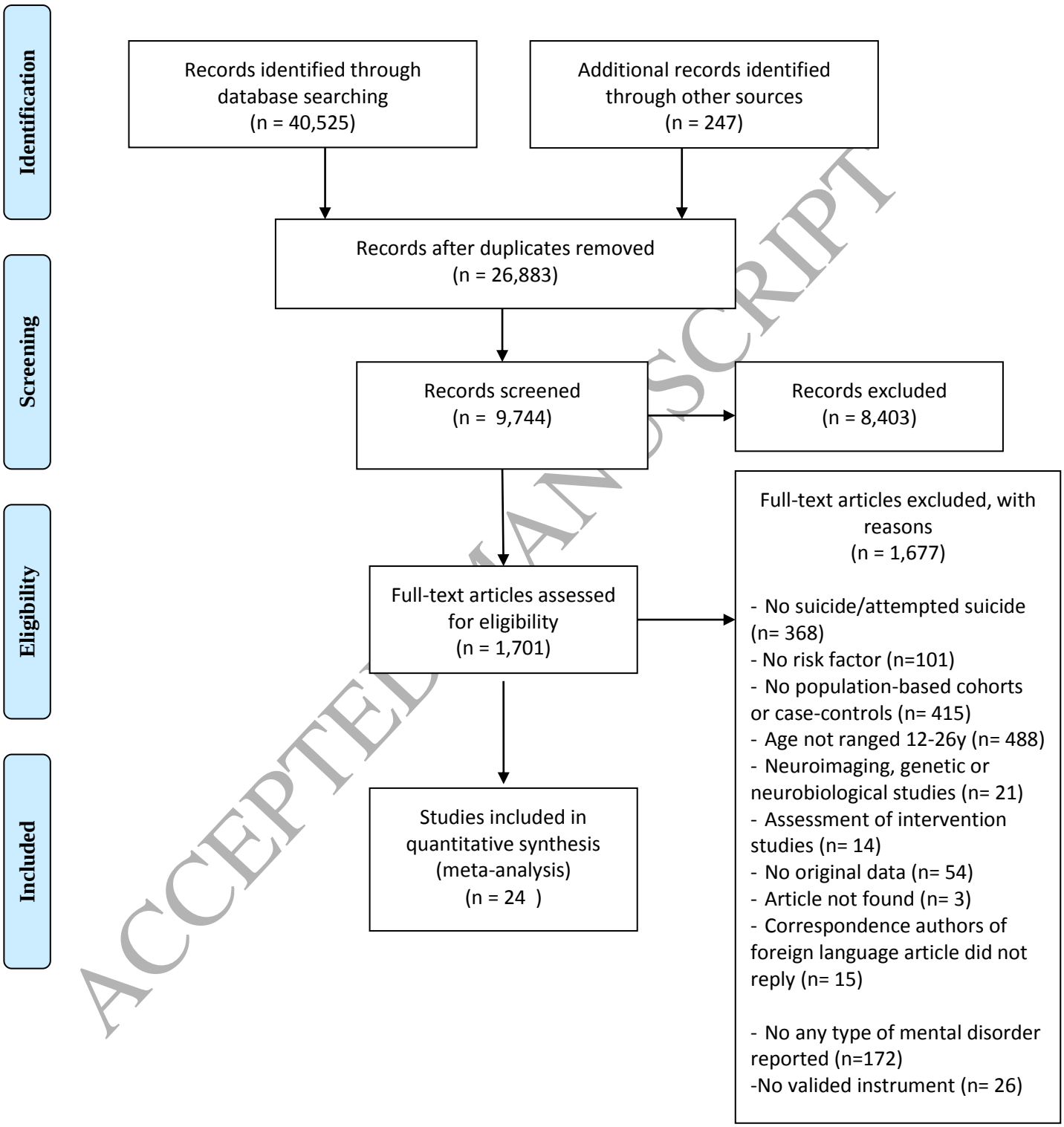
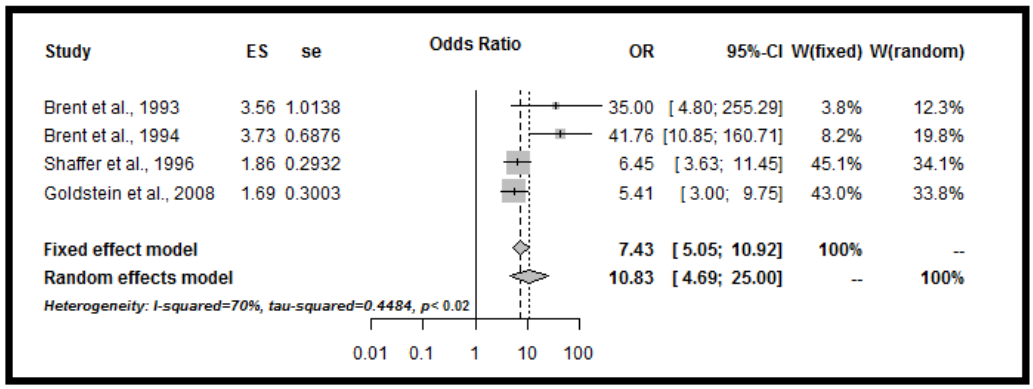
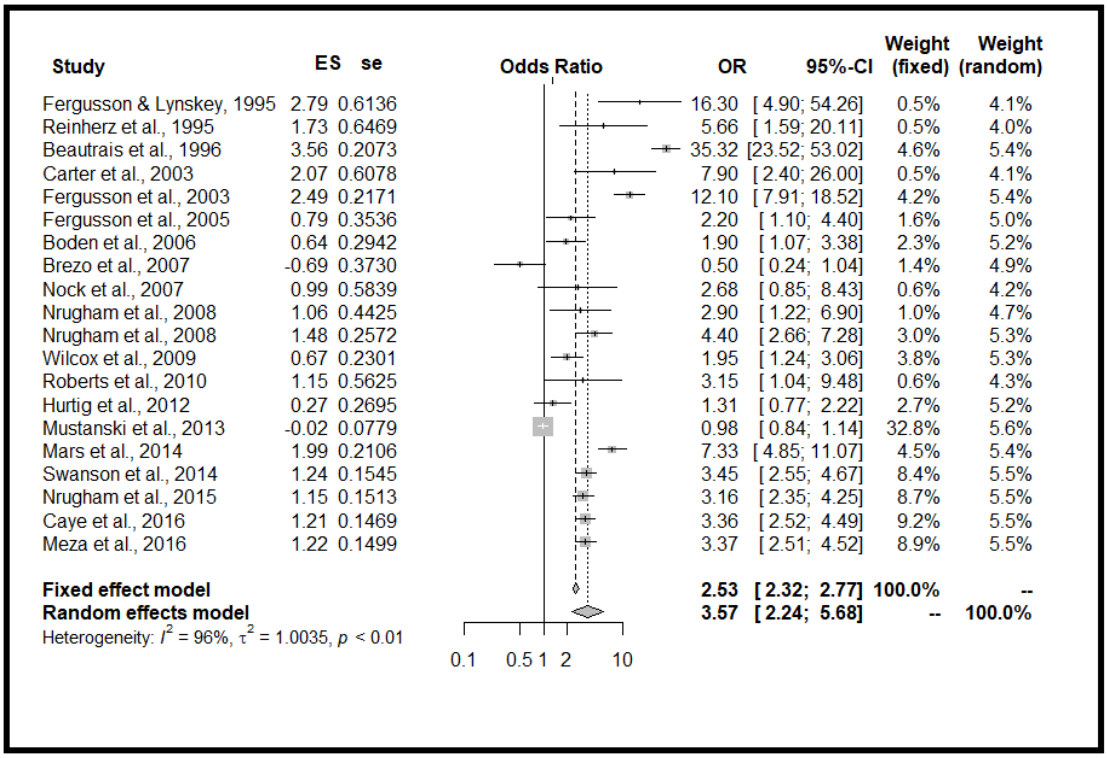


Figure 2. ***Single effect size distribution for suicidal act.***



Note. ES = effect size; se = standard error of the effect size; OR = Odds ratio; CI = confidence interval; W = within-study variance.

Figure 3. ***Single effect size distribution for suicidal attempt.***



Note. ES = effect size; se = standard error of the effect size; OR = Odds ratio; CI = confidence interval; W = within-study variance.

Table 1. Characteristics of included studies

Author	Study design	Total sample (at baseline in cohort studies)	Population	Age range (years)	Mean age (SD)	Mental disorder	Instrument	NOS Quality
Studies assessing suicide attempts								
Fergusson DM & Lynskey MT. 1995	Cohort (16 years follow-up)	954	General	16	16	Any mental disorder Mood disorder Anxiety disorder Conduct/oppositional disorder Substance use disorder	Diagnostic Interview Schedule for Children (DISC)	7
Reinherz, HZ et al. 1995	Cohort (14 years follow-up)	385	Students	18	17,9	Major depression Simple phobia Social phobia PTSD Drug abuse/dependence Alcohol abuse/dependence	NIMH Diagnostic Interview Schedule ,Version IIIR (DIS-IIIR)	7
Beautrais AL et al. 1996	Case-control	132 cases vs. 153 controls	General	13-24		Any affective disorder Any antisocial disorder Any anxiety disorder Any substance use disorder	Structured Clinical Interview for DSM-III-R (SCID)	5
Carter GL et al. 2003	Case-control	31 cases vs. 842 controls	General	18-24		Any mental disorder Any affective disorder Any anxiety disorder Personality disorder Substance use disorder	Composite International Diagnostic Interview (CIDI)	4
Fergusson DM et al. 2003	Cohort (21 years follow-up)	1265	General	15-21		Major depression	Diagnostic Interview Schedule for Children (DISC)	4
Fergusson DM et al. 2005	Cohort (7 years follow-	1006	General	21-25		Major depression	Composite International Diagnostic Interview	7

	up)						(CIDI)	
Boden JM et al. 2007	Cohort (25 years follow-up)	1265	General	16-25		GAD Panic Phobia	Composite International Diagnostic Interview (CIDI)	4
Brezo J et al. 2007	Cohort (24 years follow-up)	3017	General	15-24	21.4	Disruptive disorder	Diagnostic Interview Schedule for Children (DISC)	8
Nock MK et al. 2007	Case-control	14 cases vs. 48 control	General	12-19	17.1 (1.9)	Any mood disorder Any anxiety disorder Any eating disorder Any impulse-control disorder Any substance use disorder	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	3
Nrugham L et al. 2008	Case-control	225 cases vs. 120 controls	school-based	14-20	14.9 (0.6)	Depressive disorder	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	6
Nrugham L et al. 2008	Case-control	36 cases vs 229 controls	Students	15-20	14.9 (0.5)	Major depressive disorder Dysthimia Depressive Disorder Not Otherwise Specified	Schedule for Affective Disorders and Schizoph	8

							renia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	
Wilcox HC et al. 2009	Cohort (17 years follow-up)	2311	Students	20-23	21	Major depressive episode PTSD Alcohol abuse disorder Drug abuse or dependence	Diagnostic Interview Schedule (DSM-III-R)	5
Roberts RE et al. 2010	Cohort (1 year follow-up)	4175	General	11 to17		Any mental disorder Depressive disorder Marijuana use disorder Substance use disorder Alcohol use disorder	Diagnostic Interview Schedule for Children, Version 4 (DISC-IV)	4
Hurtig T et al. 2012	Cohort (16 years follow-up)	273	General	15-18		Depression Any anxiety diagnosis ADHD Behavioural disorder Substance use/dependence disorder	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	5
Mustanki B & Liu R. 2013	Cohort (1 year follow-up)	237	GLBT	16-20	18.6 (1.34)	Major depression disorder	Diagnostic Interview Schedule for Children (DISC)	7
Marsb B et al. 2014	Cohort (16 years follow-	4799	General	16	16	Anxiety Depression	Semi-structured DAWBA interview	6

	up)							
Swanson E.N et al. 2014	Cohort (10 years follow-up)	199	Women	16-22	19,6	ADHD-C ADHD-I	Diagnostic Interview Schedule for Children (DISC)	7
Nrugham L et al. 2015	Cohort (5 years follow-up)	345	Students	18-21	20 (0,6)	Major depressive disorder Dysthymia Alcohol disorder Conduct disorder Post-traumatic stress disorder Substance disorder	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	6
Caye A et al. 2016	Cohort (8 years follow-up)	5249	General	18-19	18	Attention-deficit/hyperactivity disorder	DSM-V clinical structured interview	
Meza JI et al. 2016	Case-control	700 cases vs 1400 controls	General	17-24	19.6	Attention-deficit/hyperactivity disorder	Diagnostic Interview Schedule for Children, 4th edition	
Studies assessing suicide								
Brent DA et al. 1993	Case-control	67 cases vs. 67 controls	General	13-19	17.1 (1.89) cases; 17.3 (1.6) controls	Any psychiatric disorder Any affective disorder Major depression Alcohol Abuse Substance abuse Drug abuse Conduct disorder	Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic and Present versions	6

							(K-SADS-E and P)	
Brent DA et al. 1994	Case-control	43 cases vs. 43 controls	General	13-19	17.4 (2.0) suicides; 17.5 (1.8) controls	Any personality disorder Antisocial Borderline Cluster A Cluster B Cluster C Compulsive Dependent Histrionic Hostility Irritability Narcissistic Paranoid Passive-Agressive Schizoid Schizotypal	Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic and Present versions (K-SADS-E and P)	7
Shaffer D et al. 1996	Case-control	120 cases vs. 147 controls	General	<20	16.9 males; 15.9 females	Mood disorder Anxiety disorder Disruptive Disorders Any substance abuse	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL)	5
Goldstein TR et al. 2008	Case-control	140 cases vs. 131 controls	General	13-19	17.3 (1.9) cases; 17.5 (1.7) controls	Any sleep disturbance	Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic and Present versions (K-SADS-E and P)	3

Table 2

Estimates for the different categories of disorders considered into this study

Outcome	Categories of disorders			
	AFF	ANX	DISR	DRUGS
Suicidal attempt				
Estimated loading (*B*)	0.46 (0.12,0.79)**	0.07 (-0.33, 0.50)	-0.37 (-1.07, 0.32)	-0.05 (-0.76, 0.67)
Overall OR	1.54 (1.21, 1.96)***	1.07 (0.78, 1.46)	0.86 (0.62, 1.21)	1.05 (0.60, 1.83)

Note. Values between brackets depict the confidence interval at 95%.

OR = odds ratio; AFF = affective disorders; ANX = anxiety disorders; DISR = disruptive disorders; DRUGS = substance abuse disorders.

* $p < .05$; ** $p < .01$; *** $p < .001$.