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**Title:** Suicidality in Huntington's disease

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# Chapter 7

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## **Suicidal ideation and subsequent completed suicide in both psychiatric and non-psychiatric populations: a meta-analysis**

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*Submitted*

## **Abstract**

*Background:* The association between suicidal ideation and subsequent completed suicide has not been firmly established in different populations and absolute suicide risks after expression are unknown.

*Aim:* To examine whether the expression of suicidal ideation predicted subsequent completed suicide in various populations.

*Method:* A meta-analysis of 73 observational studies was conducted.

*Results:* The risk for completed suicide was clearly higher in people who had expressed suicidal ideation compared with people who had not, with substantial variation between the different populations: risk ratio 3.66 (95% CI = 2.88–4.65) for psychiatric populations and 7.46 (95% CI = 5.16–10.8) for non-psychiatric populations. In contrast, the suicide risk after expression of suicidal ideation in the first year of follow-up was higher in psychiatric patients (risk = 1.21%; 95% CI = 0.64–2.28) than in non-psychiatric participants (risk = 0.26%; 95% CI = 0.10–0.73).

*Conclusion:* Expression of suicidal ideation in psychiatric patients should prompt secondary prevention strategies to reduce their substantial increased risk of suicide.

## Introduction

Almost 90% of those who died by suicide contacted a health care professional in the three months prior to their death.<sup>1</sup> Of those who had contact with a health care professional in the four weeks before their death, 22% expressed suicidal intent.<sup>2</sup> Several authors claim that expression of suicidal ideation is one of the most important predictors of completed suicide.<sup>3-5</sup> However, the association between suicidal ideation and subsequent completed suicide has not been firmly established.<sup>6</sup> Previous studies<sup>7-12</sup> and meta-analyses<sup>13-18</sup> that assessed this association were restricted to specific populations and reported varying results, with odds ratios obtained from the meta-analyses ranging from 1.5 in bipolar disorder<sup>16</sup> to 29.8 in schizophrenia.<sup>15</sup> For the general population and several other psychiatric populations the relationship between suicidal ideation and subsequent completed suicide remains unknown.<sup>6,19,20</sup> As suicidal ideation is quite common, with a lifetime prevalence of almost 10% in the general population,<sup>21</sup> it is important to know not only the relative risk but also the absolute risk of completed suicide for an individual who expresses suicidal ideation. The aforementioned meta-analyses<sup>13-18</sup> did not assess absolute risks of completed suicide. Furthermore, suicidal ideation is strongly correlated with other predictors of completed suicide like the presence of previous suicide attempts<sup>22,23</sup> and has not been firmly established as an independent predictor of completed suicide.<sup>6</sup>

Therefore, we conducted a systematic review and meta-analysis to assess whether expression of suicidal ideation predicted subsequent completed suicide in various populations, including non-psychiatric and psychiatric populations. Secondly, we aimed to estimate the absolute risks of suicide after expression of suicidal ideation in these populations and to investigate whether the expression of suicidal ideation predicted subsequent completed suicide independent of the presence of past suicide attempts.

## Method

### *Search strategy*

Ten electronic databases (PubMed, Embase, Web of science, PsycINFO, PsycARTICLES, Psychology and behavioural sciences collection, Cochrane, CINAHL, Academic search premier, and ScienceDirect) were searched until September 16, 2014, without language restrictions. A medical librarian was involved in formulating the search string (supplement S1) designed to identify studies assessing the association between the expression of suicidal ideation and completed suicide in adults.

### *Eligibility criteria*

Relevant articles fulfilling the following inclusion criteria were eligible for inclusion: 1) assessment of presence or absence of suicidal ideation as a distinct determinant (i.e. not combined with suicidal behaviour, so studies with determinants like suicidality or elevated suicide risk were not included). The presence of suicidal ideation was considered present when any form of ideation, ranging from death wish to suicide plans or threats, was expressed; 2) assessment of completed suicide (which could include open verdicts) as a distinct outcome measure; 3) comparison of suicidal ideation vs. no suicidal ideation with respect to risk of subsequent completed suicide 4) cohort or case-control study design; and 5) mean age of the study population  $\geq 18$  years.

Next, the following exclusion criteria were applied: 1) presence of suicidal ideation was assessed after a suicide attempt; 2) comparison of suicidal ideation versus suicide attempt as determinant in a cohort study; or 3) comparison of those who died by suicide and those who unsuccessfully attempted suicide as outcome in a case-control study.

For the assessment of the absolute risks of completed suicide, we included only cohort studies and nested case-control studies (with the size of the source population specified and random selection of controls from the source population) in which the number of suicides in the suicidal ideation group and the exposed person-time could be extracted or estimated.

To determine whether suicidal ideation predicted subsequent completed suicide independent of the presence of past suicide attempts, articles that assessed the effect of suicidal ideation on subsequent completed suicide adjusted for previous suicide attempts were selected.

### *Study selection*

All retrieved articles in the original search were screened independently by 2 of the 3 reviewers (AAMH, SM, and SHMP), first on title, then abstract and subsequently full-text evaluation to consider final eligibility. Disagreements with regard to final eligibility were discussed to reach consensus or, if necessary, another independent reviewer (EJG) got involved. In addition, the reference lists of eligible articles and relevant review articles identified by the search strategy were examined by one of the reviewers to search for eligible studies. When multiple publications used (partially) overlapping study populations only the largest study or, when similar, the most recent study was included.

### *Data extraction*

For each eligible article, 2 of the 3 reviewers (AAMH and SM or SHMP) independently extracted

data using a standardised form. Disagreements were discussed or another independent reviewer (EJG) got involved if needed. When information necessary to compute the effect size for the primary aim was missing, a request for the missing numbers was emailed to the corresponding author. In case of no response, the study was not included.

#### *Risk of bias assessment*

Two independent reviewers (AAMH and SM or SHMP) assessed four risk of bias aspects (selection of study population, assessment of suicidal ideation, assessment of completed suicide, and missing data) as adequate or inadequate or not reported (see supplement S2), judged on the basis of adapted items from the Newcastle-Ottawa scale<sup>24</sup> and the internal validity assessment by Altman.<sup>25</sup>

#### *Statistical analyses*

The primary outcome of this meta-analysis was the pooled unadjusted risk ratio for the association between suicidal ideation and completed suicide in a random effects model according to the method of DerSimonian and Laird.<sup>26</sup> Due to expected between study heterogeneity, e.g. due to the varying absolute risks of suicide among different populations,<sup>27</sup> the pooling of risk ratios was stratified for the following populations: affective disorders (including both in & outpatients), (former) psychiatric inpatients (mixed diagnoses), schizophrenic patients (including both in & outpatients), other mixed psychiatric populations (including substance abusers, borderline patients, and mixed diagnosis psychiatric outpatients [sometimes combined with inpatients]), general population, and a residual category that included non-psychiatric study populations that could not be grouped in one of the other categories. Studies in each subgroup were combined using a random effects model with separate estimates of tau-squared.<sup>28</sup> To pool results from different studies, odds ratios, risk ratios and incidence rate ratios were considered to approach the same value, which is reasonable given the low risk of completed suicide. When only chi-square values or p-values were given in combination with a direction of the effect, these were used to estimate risk ratios. If the given p-value was < 0.05, we assumed a p-value of 0.049. There were no eligible studies only reporting a p-value > 0.05. Since several articles reported on multiple suicidal ideation determinants (e.g. thoughts and plans separately) we computed a combined effect across these different determinants based on the mean of the related effect sizes,<sup>29</sup> so each study only contributed one effect estimate to the meta-analysis.

With regard to the risk of suicide after expression of suicidal ideation, we were most interested in the suicide risk during the first year of follow-up. Since studies had varying follow-up times, and we did not expect a constant suicide rate over time, we conducted maximum likelihood meta-regression analyses with mean study follow-up time as determinant and log<sub>e</sub>-transformed

rates of completed suicide as outcome. The obtained intercept and regression coefficient were used to calculate the  $\log_e$ -transformed rate at 1-year follow-up which was back transformed to the suicide risk during the first year of follow-up. Given the limited number of studies per population subgroup, analyses were stratified for psychiatric and non-psychiatric populations only. When one article assessed suicidal ideation at multiple time points (e.g. current and lifetime), we only included the determinant that assessed suicidal ideation closest to baseline.

In order to assess whether suicidal ideation predicted completed suicide independently of previous attempts, the past suicide attempt-adjusted risk ratios were extracted and used for estimation.

To check the robustness of the results, we restricted the analyses to 1) studies with a low risk of bias (see supplement S2), 2) to cohort studies (for the primary research aim only), and 3) studies that assessed suicidal ideation at baseline or in the preceding month (for the secondary research aim only). In addition, we were interested in the results in different subgroups and stratified analyses of the primary outcome for studies with short ( $\leq$  1-year) versus long ( $>$  1-year) timeframe between expression of suicidal ideation and completed suicide and suicidal ideation assessment method. Maximum likelihood meta-regression was applied to examine the effects of mean age and gender in the study populations.

Heterogeneity was assessed using the  $I^2$  statistic, publication bias by inspecting the funnel plot and Egger's test for funnel plot asymmetry. A p-value  $<$  0.05 was considered statistically significant. Statistical analyses were performed using Comprehensive Meta-analysis software version 2.0.064 ([www.meta-analysis.com](http://www.meta-analysis.com)).

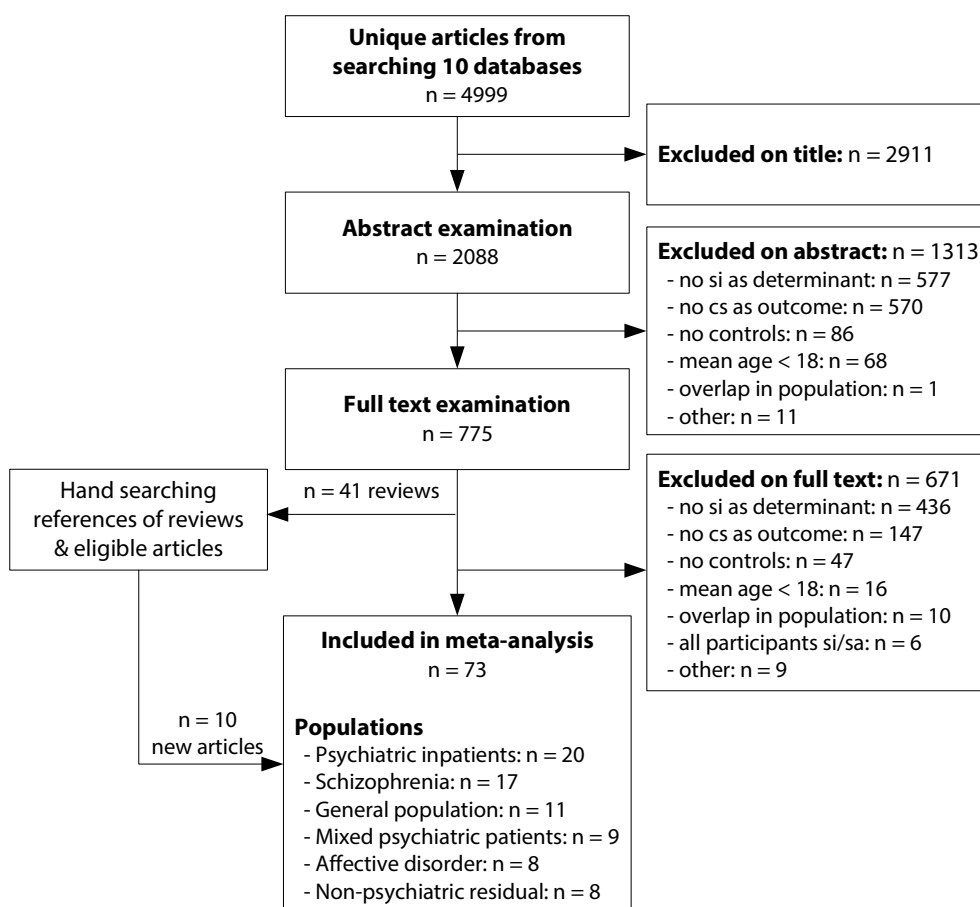
## Results

### *Literature search and study characteristics*

The literature search identified 4999 unique articles: 73 articles were finally included (Figure 1). Most studies ( $n = 20$ ) investigated suicide in psychiatric inpatients (mixed diagnoses), others in schizophrenia (both in- and outpatients) ( $n = 17$ ), general population ( $n = 11$ ), mixed psychiatric populations ( $n = 9$ ; including 3 studies on substance abusers, 2 on borderline patients, 2 on mixed diagnosis psychiatric in & outpatients, and 2 on mixed diagnosis psychiatric outpatients), affective disorder (both in- and outpatients) ( $n = 8$ ), or in the non-psychiatric residual category ( $n = 8$ ; including 2 studies on military, 1 on veterans, 1 on stalkers, 1 study on HIV infected males, 1 on survivors of childhood cancer, 1 on prisoners, and 1 on emergency department

visitors) (Figure 1). Together these studies included 4,445,979 participants (median 203; range 14–4,045,993), with a total of 7462 completed suicides (median 60; range 3–1429). Reported mean age ranged from 18.3–76.2 years, and studies included median 41.6% (range 0–67.5) females (see supplementary Table 1 in supplement S3).

The majority of included studies were (nested) case-control studies ( $n = 50$ , 68.5%). In only 23 studies the absolute risk of completed suicide could be extracted. None of the 73 eligible articles assessed the effect of suicidal ideation on completed suicide with sole adjustment for



**Figure 1.** Flowchart of the study selection process.

Si denotes suicidal ideation; cs, completed suicide; sa, suicide attempts.

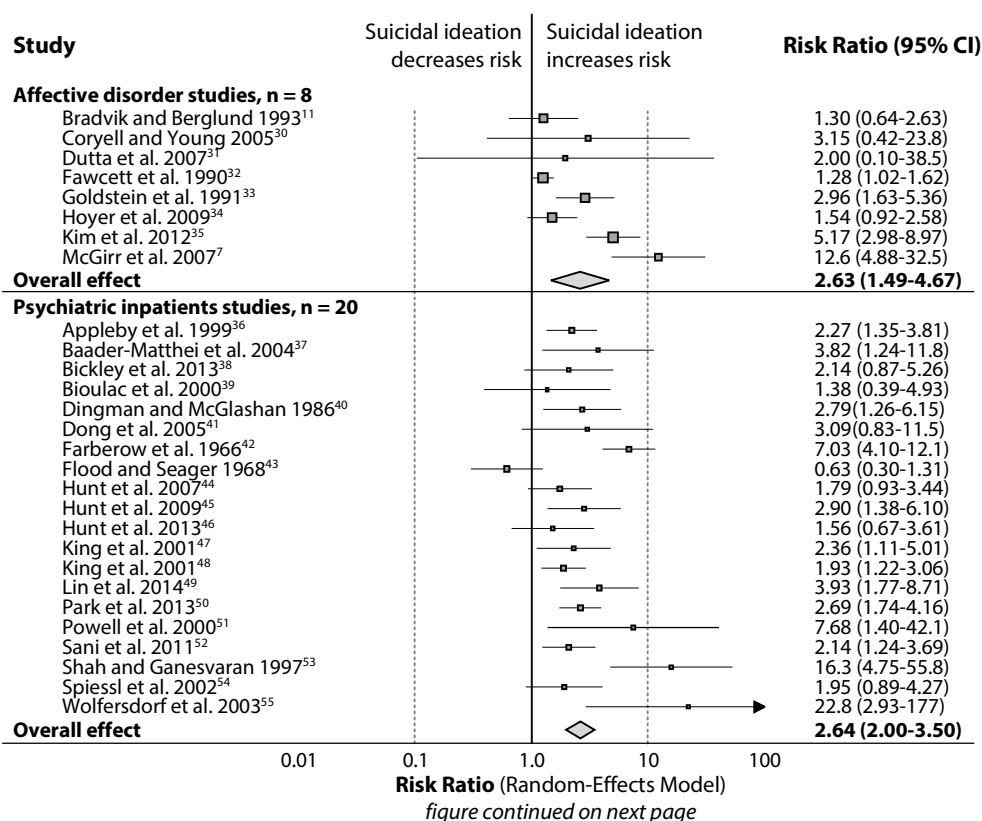
Databases searched: PubMed, Embase, Web of science, PsycINFO, PsycARTICLES, Psychology and behavioural sciences collection, Cochrane, CINAHL, Academic Search Premier, and Science Direct. Independent screening by 2 reviewers, disagreements with regard to final eligibility were discussed.

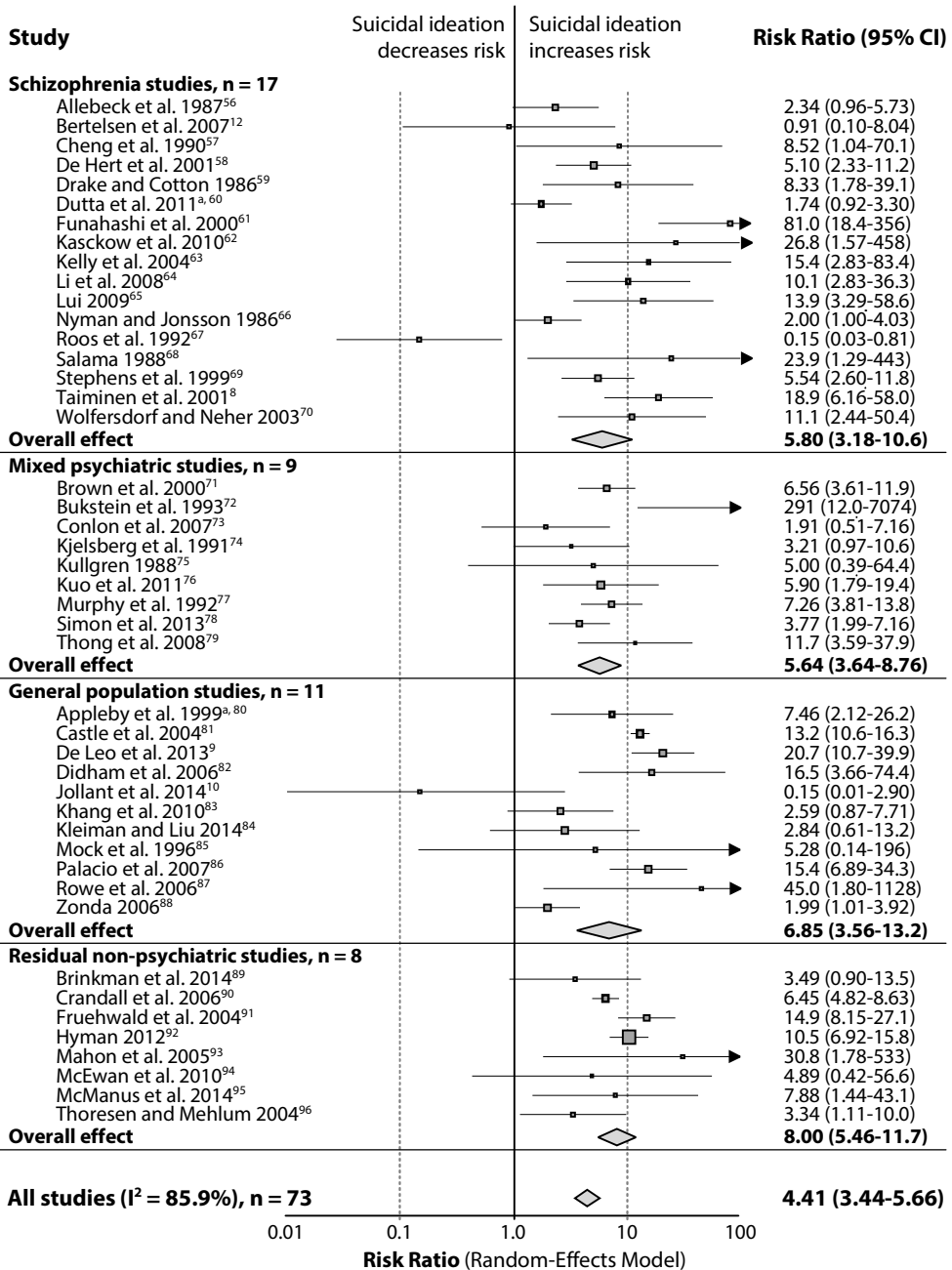


previous suicide attempts. However, there were 42 studies that applied a multivariable model, but only 26 adjusted for previous attempts as a separate determinant in this model.

### *Association between suicidal ideation and subsequent completed suicide*

For all population subgroups investigated in this meta-analysis, the pooled risk of suicide was significantly higher in study participants who had expressed suicidal ideation compared with study participants who had not. Whereas the overall risk ratio (RR) was 4.41 (95% CI = 3.44–5.66), the risk ratios per population subgroup varied substantially. The risk ratio was highest in the non-psychiatric residual subgroup (RR = 8.00; 95% CI = 5.46–11.7), followed by the general population (RR = 6.85; 95% CI = 3.56–13.2), schizophrenia (RR = 5.80; 95% CI = 3.18–10.6), mixed psychiatric patients (RR = 5.64; 95% CI = 3.64–8.76), psychiatric inpatients (RR = 2.64; 95% CI = 2.00–3.50), and affective disorder (RR = 2.63; 95% CI = 1.49–4.67) (Figure 2). Overall, the risk ratio was 3.66 (95% CI = 2.88–4.65) in psychiatric populations and 7.46 (95% CI = 5.16–10.8) in non-psychiatric populations (data not shown).





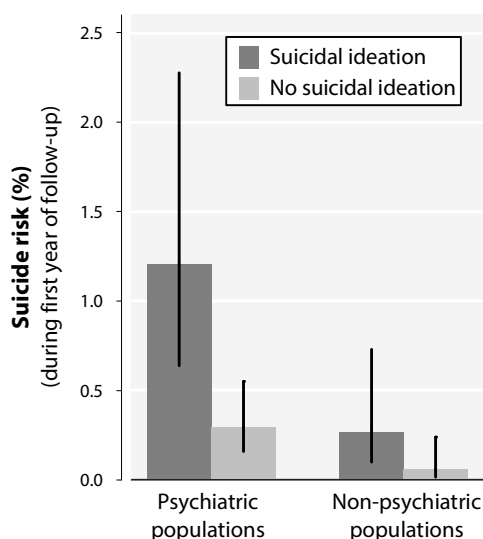
**Figure 2.** Forest plot showing the association between si and subsequent completed suicide. CI denotes confidence interval; si, suicidal ideation.

<sup>a</sup> Authors provided additional data to compute effect size.

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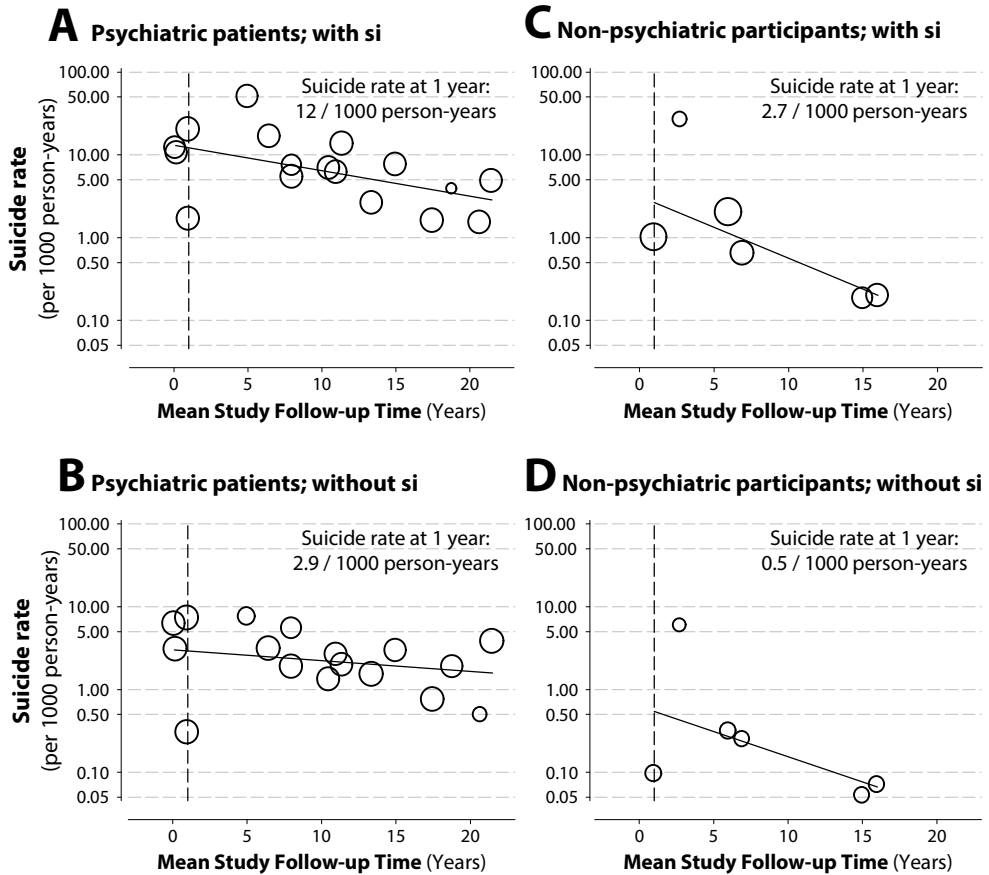
*Risk of completed suicide*

Although the psychiatric subgroups had the lowest risk ratios, meta-regression analyses showed the suicide risk was highest in the psychiatric subgroups who had expressed suicidal ideation (risk during first year of follow-up = 1.21%; 95% CI = 0.64–2.28). This was clearly higher than the suicide risk in psychiatric patients who had not expressed suicidal ideation (risk during first year of follow-up = 0.29%; 95% CI = 0.15–0.55). While the difference between study participants who had expressed suicidal ideation and study participants who had not was relatively larger in the non-psychiatric subgroups, the suicide risk in non-psychiatric populations was lower. The suicide risk during the first year of follow-up was 0.26% (95% CI = 0.10–0.73) in non-psychiatric study participants who had expressed suicidal ideation and 0.05% (95% CI = 0.01–0.24) in non-psychiatric study participants who had not (Figure 3 and Figure 4). When grouping all studies, the suicide risk during the first year of follow-up after expression of suicidal ideation was 0.76% (95% CI = 0.33–1.77) (data not shown). The meta-regression line showed that in all populations the suicide rate decreased as time progressed (Figure 4).



**Figure 3.** Bar chart showing the suicide risk (%) during first year of follow-up.

Results specified separately for study participants who had expressed suicidal ideation and study participants who had not, stratified for psychiatric and non-psychiatric populations. Lines indicate 95% confidence interval. Percentages calculated using maximum likelihood meta-regression analyses with mean study follow-up time as determinant and  $\log_e$ -transformed rates of completed suicide as outcome (see Figure 4).



**Figure 4.** Meta-regression of mean study follow-up time on suicide rate.

SI indicates suicidal ideation. Maximum likelihood meta-regression analyses with mean study follow-up time as determinant and  $\log_e$ -transformed rates of completed suicide as outcome presented on logarithmic scales. The bubble size is proportional to the study's weight. Vertical line indicates 1-year follow-up.

The suicide risk can be calculated using the following formulas: suicide risk (during first year of follow-up) =  $1 - e^{-(\text{rate per person-year at year } 1)}$ . A and B: Psychiatric subgroup included: Bradvik and Berglund 1993;<sup>11</sup> Coryell and Young 2005;<sup>30</sup> Dutta et al. 2007;<sup>31</sup> Goldstein et al. 1991;<sup>33</sup> Bioulac et al. 2000;<sup>39</sup> Dingman and McGlashan 1986;<sup>40</sup> Lin et al. 2014;<sup>49</sup> Park et al. 2013;<sup>50</sup> Sani et al. 2011;<sup>52</sup> Spiessl et al. 2002;<sup>54</sup> Allebeck et al. 1987;<sup>56</sup> de Hert et al. 2001;<sup>58</sup> Drake and Cotton 1986;<sup>59</sup> Dutta et al. 2011;<sup>60</sup> Stephens et al. 1999;<sup>69</sup> Kuo et al. 2011;<sup>76</sup> Simon et al. 2013;<sup>78</sup> C and D: Non-psychiatric subgroup included: Khang et al. 2010;<sup>83</sup> Kleiman and Liu 2014;<sup>84</sup> Brinkman et al. 2014;<sup>89</sup> Crandall et al. 2006;<sup>90</sup> Hyman 2012;<sup>92</sup> McEwan et al. 2010.<sup>94</sup>

### *Risk of bias assessment & sensitivity analyses*

Eighty-five percent of the studies adequately selected the study population, 68% adequately assessed the presence of suicidal ideation, 88% adequately assessed completed suicide, and 66% had < 10% missing information (supplement S2 and supplementary Table 1 in supplement S3). When restricting the analyses to studies that scored 'adequate' on all four items ( $n = 31$ , 42.5%), the pooled risk ratio (which was 4.41 in the main analysis) decreased slightly to 3.61 (95% CI = 2.81–4.64) and the overall suicide risk during the first year of follow-up (which was 0.76% in the main analysis) remained similar (risk during first year of follow-up = 0.78%; 95% CI = 0.29–2.12). In addition, restricting the primary analysis to cohort studies resulted in a slight decrease in the risk ratio (RR = 3.44; 95% CI = 2.35–5.03). Restricting the secondary analysis to studies that assessed suicidal ideation in the month around baseline resulted in a similar risk (risk during first year of follow-up = 0.75%; 95% CI = 0.31–1.84).

### *Is suicidal ideation an independent predictor of completed suicide?*

Of all studies that used a multivariable model for the prediction of suicide and adjusted for (among other predictors) the presence of a previous suicide attempt ( $n = 26$ ), only 12 reported the adjusted effect size of suicidal ideation. In 9 of these studies suicidal ideation was a significant independent predictor of completed suicide. The other 14 studies that included previous attempts in their multivariable model either did not include suicidal ideation as a separate predictor ( $n = 6$ ), or did include suicidal ideation but did not report the adjusted effect size ( $n = 8$ ), which was non-significant in 7 of these studies. While in at least 9 studies suicidal ideation was a significant independent predictor of completed suicide, which is significantly more than expected by chance, the 12 adjusted effect sizes were not pooled due to large underreporting of mainly non-significant results.

### *Subgroup analyses*

There was considerable heterogeneity ( $I^2$  for overall risk ratio = 86%), even when stratified for specific populations. Results of subgroup analyses regarding the timeframe between the expression of suicidal ideation and completed suicide and suicidal ideation assessment method can be found in supplementary Figure 1 in supplement S4, just like the results of the meta-regression analyses regarding age and gender.

### *Publication bias*

The funnel plot (supplementary Figure 2 in supplement S5) computed for the primary research question showed a rather symmetrical funnel plot. Egger's test indicated no funnel plot asymmetry (2-tailed  $p$ -value = 0.82).

## Discussion

Meta-analysing 73 eligible studies showed that overall, people expressing suicidal ideation are 4 times more likely to die by suicide than people not expressing suicidal ideation, with a suicide risk during the first year of follow-up of 1.2% in psychiatric populations and 0.26% in non-psychiatric populations. Effect estimates differed substantially among different populations: all in all, psychiatric populations showed the highest absolute suicide risks after expression of suicidal ideation but lowest relative risks, whereas the non-psychiatric populations showed the highest relative risks but lowest absolute risks.

The results of this meta-analysis are in line with previous meta-analyses on suicidal ideation and subsequent completed suicide.<sup>13-15;17;18</sup> The highest relative risk was found in a meta-analysis restricted to schizophrenic patients<sup>15;18</sup> followed by meta-analyses restricted to psychiatric inpatients<sup>13;14</sup> and depressed patients.<sup>17;18</sup> Remarkably one recent meta-analysis<sup>18</sup> reported that the association between suicidal ideation and completed suicide was not significant in patients with a mood disorder, while the current meta-analysis reports a significant association. This is probably explained by the broader definition of suicidal ideation that was applied in the current study, also including expression of death ideation or suicide plans, and the fact that we excluded studies that compared expression of suicidal ideation in suicide completers versus attempters, while this previous meta-analysis included such studies.<sup>18</sup> Unfortunately, none of the previous meta-analyses<sup>13-18</sup> assessed the absolute risks of suicide.

The expression of suicidal ideation is also a significant independent predictor of completed suicide, given the high number of studies that reported this. However, the effect size remains unknown, as past suicide attempt-adjusted risk ratios could not be pooled. Underreporting of non-significant effect sizes would likely have yielded a biased overestimation of the risk ratio. Many studies included in our meta-analysis did develop a prediction model for suicide, although it is widely accepted that it is very difficult to accurately predict suicide for an individual patient,<sup>97</sup> and there is a lot of debate on whether or not clinical risk categorization is helpful in preventing completed suicide.<sup>98;99</sup> It was striking that only less than 60% of these studies included previous suicide attempts as a predictor, whereas this has been reported as one of the most important independent predictors of completed suicide.<sup>98</sup> Future studies on suicide risk assessment should therefore include known predictors from the literature (e.g., previous suicide attempts) rather than only selecting predictors by univariable screening in the developmental dataset.<sup>100</sup>

### *Strengths and limitations*

A major strength of our paper was the attempt to provide risk estimates for different subgroups. Moreover, we strictly excluded studies that might have combined suicidal ideation with behaviour, and included many studies for the primary research aim. There are also limitations that need to be considered. First, the majority of studies only provided long-term follow-up results, while the short-term risk has most clinical value. Although the provided suicide risks should be interpreted with caution due to the declining rates over time and the limited number of studies, especially with short-term follow-up, that could be included in the meta-regression analyses, results clearly show the risk of suicide is higher after expression of suicidal ideation, especially in psychiatric patients. Future studies should focus on short-term suicide risk in the different psychiatric populations. Second, only part of the large amount of heterogeneity could be explained for; several patients characteristics that would be interesting in exploring/explaining this heterogeneity, like duration of suicidal ideation<sup>101</sup> or behavioural traits<sup>102</sup> were not provided in the studied articles. In addition, study level confounding<sup>103</sup> might have influenced the results of our subgroup analyses, e.g. resulted in a significant effect of gender on the association between suicidal ideation and completed suicide, as the percentage of females was lower in certain high risk population subgroups like schizophrenia. Third, the varying or lacking definitions of suicidal ideation in the eligible studies might have been another source of unexplained and unmeasurable heterogeneity. Clear definitions of suicidal ideation are necessary,<sup>104</sup> as different assessment methods may result in different suicide ideation prevalence numbers, even in the same population at the same time point.<sup>105</sup> Also different studies assessed suicidal ideation during different time periods, but sensitivity analyses showed that restricting the meta-regression analysis to studies that assessed suicidal ideation at baseline or the month before resulted in a similar suicide risk. Fourth, some required study parameters could not be directly extracted from the original articles. For example the exposed person-years were conservatively estimated when possible, which could have resulted in an underestimation of the suicide risk.

### *Implications for clinical practice*

For clinical psychiatric care, it is important to inquire about suicidal ideation in psychiatric patients given the substantial risk after expression of suicidal ideation, especially in the first period after expression. Although the relative risk was highest in non-psychiatric populations, the suicide risk after expression of suicidal ideation was lower than in psychiatric populations and decreased faster over time. However, even in psychiatric patients suicidal ideation assessment should be placed in perspective as the suicide risk during the first year of follow-up among psychiatric patients who had not expressed suicidal ideation was 0.29%, which was similar to the suicide risk in non-psychiatric persons who had expressed suicidal ideation.

Clinicians know they should be alert when a psychiatric patient expresses suicidal ideation<sup>106</sup> and the suicide risks provided in this meta-analysis can help clinicians in their stepped care approach to decide whether the considered secondary prevention measure (ranging from further exploring suicidal thoughts to a compulsory admission) is proportionate to the risk of suicide.

In a patient who expresses suicidal ideation, follow-up inquiries are needed about the nature of these thoughts and the assessment of other known risk factors for suicide.<sup>107</sup> As patients will not always express suicidal ideation spontaneously,<sup>97</sup> it is important to ask them about suicidal thoughts. Actually, asking patients about suicidal ideation can reduce future suicidal ideation and follow-up inquiries can benefit long-term mental health.<sup>108</sup> Patients often feel relieved by having an opportunity to talk about their suicidal ideas,<sup>109</sup> especially if clinicians take time, show empathy, and acknowledge the suicidal feelings.<sup>110</sup> Remarkably, in several of the included studies that assessed the presence of suicidal ideation in medical records, this information was missing. This means that it was unavailable to clinicians and appropriate care might have been unnecessarily withheld from these patients.<sup>48</sup>

Fortunately, the majority of patients with suicidal ideation do not die by suicide. Nevertheless, assessment of suicidal ideation is of priority in people with psychiatric illnesses and when a patient expresses suicidal ideation, prompt secondary prevention strategies are necessary to reduce their substantial increased risk of suicide.

## Acknowledgments

We would like to thank medical librarian J.W. Schoones, Walaeus Library, Leiden University Medical Center for his help in conducting the literature search. In addition, we would like to thank the authors that provided additional information on their studies.



## Supplements

### Supplement S1. Search strategy

The following search strategy was used in Pubmed on September 16th, 2014. Combining the results of search strategy part 1 and part 2 with OR resulted in 3416 references in PubMed. In addition, Embase, Web of Science, PsycINFO, PsycARTICLES, Psychology and Behavioural Sciences Collection, COCHRANE, CINAHL, Academic Search Premier, ScienceDirect were searched for eligible articles (total 4999 references).

#### *Search strategy part 1 focusing on prediction of suicide in adults*

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*Search strategy part 2 focusing on suicidal ideation and suicide in adults*

((("Suicidal Ideation"[mesh] OR "suicide ideation"[all fields] OR "suicidal ideation"[all fields] OR "suicide thoughts"[all fields] OR "suicide thought"[all fields] OR "suicidal thoughts"[all fields] OR "suicidal thought"[all fields] OR "suicide idea"[all fields] OR "suicide ideas"[all fields] OR "suicide ideator"[all fields] OR "suicide ideators"[all fields] OR "suicidal idea"[all fields] OR "suicidal ideas"[all fields] OR "suicidal ideator"[all fields] OR "suicidal ideators"[all fields] OR "suicidality"[all fields] OR "suicidal tendencies"[all fields] OR "death wishes"[all fields] OR "suicidal tendency"[all fields] OR "death wish"[all fields] OR "talk of suicide"[all fields] OR "threat of suicide"[all fields] OR "suicidal communication"[all fields]) AND (predict\*[all fields] OR "predict"[all fields] OR "predictors"[all fields] OR "predictor"[all fields] OR "predictive"[all fields] OR "predicted"[all fields] OR "prediction"[all fields] OR "predictions"[all fields] OR predict\*[all fields] OR "trajectory"[all fields] OR "course"[all fields] OR "Time factors"[mesh] OR "Risk Factors"[mesh] OR "Risk"[mesh] OR "Probability"[mesh] OR "Prognosis"[mesh] OR prognos\*[all fields] OR "time factors" [all fields] OR "risk factor"[all fields] OR "risk factors"[all fields]) AND ("Suicide"[mesh:noexp] OR "Suicide, Attempted"[mesh] OR "suicide"[all fields] OR "completed suicide"[all fields] OR "eventual suicide"[all fields] OR "completed suicides"[all fields] OR "eventual suicides"[all fields] OR "later suicide"[all fields] OR "later suicides"[all fields] OR "subsequent suicide"[all fields] OR "subsequent suicides"[all fields] OR "suicide"[all fields] OR "suicides"[all fields] OR "suicidal behaviour"[all fields] OR "suicidal behaviour"[all fields] OR "suicidal behaviours"[all fields] OR "suicidal behaviours"[all fields] OR "suicide behaviour"[all fields] OR "suicide behaviour"[all fields] OR "suicide behaviours"[all fields] OR "suicide behaviours"[all fields]) AND ("Adult"[mesh] OR "adult"[all fields] OR "adults"[all fields])) OR ((("Suicidal Ideation"[mesh] OR "suicide ideation"[all fields] OR "suicidal ideation"[all fields] OR "suicide thoughts"[all fields] OR "suicide thought"[all fields] OR "suicidal thoughts"[all fields] OR "suicidal thought"[all fields] OR "suicide idea"[all fields] OR "suicide ideas"[all fields] OR "suicide ideator"[all fields] OR "suicide ideators"[all fields] OR "suicidal idea"[all fields] OR "suicidal ideas"[all fields] OR "suicidal ideator"[all fields] OR "suicidal ideators"[all fields] OR "suicidality"[all fields] OR "suicidal tendencies"[all fields] OR "death wishes"[all fields] OR "suicidal tendency"[all fields] OR "death wish"[all fields] OR "talk of suicide"[all fields] OR "threat of suicide"[all fields] OR "suicidal communication"[all fields]) AND (predict\*[all fields] OR "predict"[all fields] OR "predictors"[all fields] OR "predictor"[all fields] OR "predictive"[all fields] OR "predicted"[all fields] OR "prediction"[all fields] OR "predictions"[all fields] OR predict\*[all fields] OR "trajectory"[all fields] OR "course"[all fields] OR "Time factors"[mesh] OR "Risk Factors"[mesh] OR "Risk"[mesh] OR "Probability"[mesh] OR "Prognosis"[mesh] OR

prognos\*[all fields] OR "time factors" [all fields] OR "risk factor"[all fields] OR "risk factors"[all fields]) AND ("Suicide"[mesh:noexp] OR "Suicide, Attempted"[mesh] OR "suicide"[all fields] OR "completed suicide"[all fields] OR "eventual suicide"[all fields] OR "completed suicides"[all fields] OR "eventual suicides"[all fields] OR "later suicide"[all fields] OR "later suicides"[all fields] OR "subsequent suicide"[all fields] OR "subsequent suicides"[all fields] OR "suicide"[all fields] OR "suicides"[all fields] OR "suicidal behaviour"[all fields] OR "suicidal behaviour"[all fields] OR "suicidal behaviours"[all fields] OR "suicidal behaviours"[all fields] OR "suicide behaviour"[all fields] OR "suicide behaviour"[all fields] OR "suicide behaviours"[all fields] OR "suicide behaviours"[all fields]) NOT ("Adolescent"[mesh] OR "Child"[mesh]) NOT "Adult"[mesh])) AND ("Case-Control Studies"[mesh] OR "Case-Control"[all fields] OR "Case-Controlled"[all fields] OR "Retrospective"[all fields] OR Retrospectiv\*[all fields] OR "Retrospective Studies"[all fields] OR "Retrospective Study"[all fields] OR "Cohort Studies"[mesh] OR "Cohort"[all fields] OR "Cohorts"[all fields] OR "Longitudinal Studies"[all fields] OR "Longitudinal Study"[all fields] OR "Follow-Up Studies"[all fields] OR "Follow-Up Study"[all fields] OR "Follow-Up"[all fields] OR "Prospective Studies"[all fields] OR "Prospective Study"[all fields] OR "Multivariate Analysis"[Mesh] OR "Multivariate"[all fields])

**Supplement S2.** Risk of bias assessment

Adapted from Newcastle-Ottawa scales<sup>24</sup> and framework by Altman<sup>25</sup>

*Case-control studies*

1. Selection of study population
  - (1) Adequate: Cases are a consecutive or obviously representative series of cases. Controls are a randomly selected sample from the cases' source population.
  - (2) Inadequate or not reported: Selected cases are not representative or controls are not randomly selected from cases' source population.
  
2. Assessment of determinant (presence of suicidal ideation)
  - (1) Adequate: description of suicidal ideation assessment is provided and is the same for cases and controls, and information on presence of suicidal ideation is obtained from a source that was blind for the outcome (e.g. reported in medical record at time before suicide).
  - (2) Inadequate or not reported: no description of suicidal ideation assessment provided, or assessment is different for cases and controls, or information on presence of suicidal ideation came from a source that was not blind for the outcome (e.g. asked to next of kin after suicide).
  
3. Assessment of outcome (completed suicide)
  - (1) Adequate: Use of death certificates/coroners verdicts/medical verdicts/registries to avoid misclassification of suicides.
  - (2) Inadequate or not reported: No use of death certificates/coroners verdicts/medical verdicts/registries, misclassification of suicides likely.
  
4. Missing information on determinant (presence of suicidal ideation)
  - (1) Adequate: No or small number of participants with missing information on determinant:  $\leq 10\%$ .
  - (2) Inadequate or not reported: Large number of participants with missing information on determinant:  $> 10\%$ . Participants who were eligible for participation but had missing medical files or no informant that was willing to provide information on the presence of suicidal ideation were considered as participants with missing information.

*Cohort studies*

1. Selection of study population
  - (1) Adequate: Participants are a random (consecutive) sample of eligible patients, most

important aspect: non-exposed cohort drawn from same community as the exposed cohort and at the same time point in course of disease.

(2) Inadequate or not reported: Participants are not a random sample of eligible patients, especially inadequate when non exposed cohort is drawn from different source or at different time point in course of disease.

2. Assessment of determinant (presence of suicidal ideation)

(1) Adequate: description of suicidal ideation assessment provided.

(2) Inadequate: no description of suicidal ideation assessment provided.

3. Assessment of outcome (completed suicide)

(1) Adequate: Use of death certificates/coroners verdicts/medical verdicts/registries to avoid misclassification of suicides.

(2) Inadequate or not reported: No use of death certificates/coroners verdicts/medical verdicts/registries, misclassification of suicides likely.

4. Missing information on follow-up

(1) Adequate: no or small number of participants lost to follow-up:  $\leq 10\%$ . If death registries were used with expected coverage  $> 90\%$ , this item was scored adequate.

(2) Inadequate or not reported: large number of participants lost to follow-up:  $>10\%$ .

*Scoring system*

Total score is computed by adding scores on four items (range 0–4 points).

*Low* risk of bias: total score 4 points

*Medium* risk of bias: total score 5-6 points

*High* risk of bias: total score 7-8 points

**Supplement S3.** Literature table  
**Supplementary Table 1.** Details of studies included in the meta-analysis for answering the primary research aim.

First author, year	Study design <sup>a</sup>	Sample size	Suicides	Age (years) <sup>b</sup>	% female	SI assessment <sup>c</sup>	Q1 <sup>d</sup>	Q2	Q3	Q4
<i>Affective disorder</i>										
Bradvik & Berglund 1993 <sup>11</sup>	Matched nested cc	178	89	46.7	57.3	Medical record	1	1	1	1
Coryell & Young 2005 <sup>e,30</sup>	Cohort	785	33	38.8	67.5	Interview part.	1	1	1	1
Dutta et al. 2007 <sup>31</sup>	Cohort	239	8	33.2	56.6	Medical record	1	1	1	1
Fawcett et al. 1990 <sup>32</sup>	Cohort	954	32	38.1	58.0	Interview part.	1	1	1	?
Goldstein et al. 1991 <sup>33</sup>	Cohort	1906	46	41.2	60.7	Medical record	1	1	1	1
Hoyer et al. 2009 <sup>34</sup>	Matched cc	270	135	44% ≤ 55	51.1	Medical record	1	1	1	1
Kim et al. 2012 <sup>35</sup>	Matched nested cc	636	324	58	12.4	Medical record	1	1	1	1
McGirr et al. 2007 <sup>7</sup>	Case control	237	156	42.5	22.8	Interview NOK	1	2	1	2
<i>Psychiatric inpatients</i>										
Appleby et al. 1999 <sup>36</sup>	Matched cc	298	149	med 38	35.7	Medical record	1	1	1	1
Baader-Matthei et al. 2004 <sup>37</sup>	Matched nested cc	64	32	46.1	46.9	Medical record	1	1	1	1
Bickley et al. 2013 <sup>38</sup>	Case control	200	100	med 42	44	Quest. clinician	1	2	1	1
Bioulac et al. 2000 <sup>39</sup>	Cohort	200	10	41.2	54	Interview part.	1	1	2	1
Dingman & MacGlashan 1986 <sup>40</sup>	Cohort	460	38	?	54.2	Medical record	1	1	2	1
Dong et al. 2005 <sup>41</sup>	Matched nested cc	184	92	41.1	47.8	Medical record	1	1	1	1
Farberow et al. 1966 <sup>42</sup>	Nested cc	438	218	40.1	0	Medical record	1	1	1	1
Flood and Seager 1968 <sup>43</sup>	Matched nested cc	216	73	49	65	Medical record	1	1	1	2
Hunt et al. 2007 <sup>44</sup>	Matched nested cc	444	222	med 39	42.8	Quest. clinician	1	2	1	1

Table continued on the next page.

First author, year	Study design <sup>a</sup>	Sample size	Suicides	Age (years) <sup>b</sup>	% female	SI assessment <sup>c</sup>	Q1 <sup>d</sup>	Q2	Q3	Q4
Hunt et al. 2009 <sup>45</sup>	Matched nested cc	476	238	med 39.5	41.6	Quest. clinician	1	2	1	1
Hunt et al. 2013 <sup>46</sup>	Matched nested cc	214	107	med 40	40.2	Quest. clinician	1	2	1	1
King et al. 2001 <sup>47</sup>	Matched nested cc	165	59	?	45.8	Medical record	1	1	1	2
King et al. 2001 <sup>48</sup>	Matched nested cc	665	234	44.0	37.5	Medical record	1	1	1	2
Lin et al. 2014 <sup>49</sup>	Matched nested cc	203	41	34	49.3	Medical record	1	1	1	1
Park et al. 2013 <sup>50</sup>	Cohort	8403	96	41	57.2	Medical record	1	1	1	1
Powell et al. 2000 <sup>51</sup>	Matched nested cc	187	97	43.5	50.8	Medical record	1	1	1	2
Sani et al. 2011 <sup>52</sup>	Matched nested cc	288	96	?	44.8	Psychol. autopsy	1	2	?	1
Shah and Ganesvaran 1997 <sup>53</sup>	Matched nested cc	120	60	med 32 (s)	45	Medical record	1	1	1	2
Spießlet al. 2002 <sup>54</sup>	Cohort	21062	30	47.1	46.5	Medical record	1	1	1	1
Wolfersdorf et al. 2003 <sup>55</sup>	Matched nested cc	128	64	45.2	36	Medical record	1	2	1	?
<i>Schizophrenia</i>										
Allebeck et al. 1987 <sup>56</sup>	Nested cc	96	32	36.8	52.1	Medical record	1	1	1	?
Bertelsen et al. 2007 <sup>12</sup>	Cohort	547	7	26	41	Interview part.	1	1	1	1
Cheng et al. 1990 <sup>57</sup>	Matched nested cc	148	74	31.1	41.9	Medical record	1	1	?	1
de Hert et al. 2001 <sup>58</sup>	Matched nested cc	126	63	28.6	22.2	Psychol. autopsy	1	2	?	1
Drake and Cotton 1986 <sup>59</sup>	Cohort	104	15	31.4	45.1	Medical record	1	1	1	1
Dutta et al. 2011 <sup>60</sup>	Cohort	2132	51	36.1	47.9	Medical record	1	1	1	1
Funahashi et al. 2000 <sup>61</sup>	Matched cc	160	80	35.6	23.8	Medical record	2	1	1	?
Kasckow et al. 2010 <sup>62</sup>	Case control	98	74	45.0	31.6	Interview NOK	2	2	1	2
Kelly et al. 2004 <sup>63</sup>	Case control	97	15	48.1	35.1	Psychol. autopsy	2	2	?	2
Li et al. 2008 <sup>64</sup>	Matched nested cc	128	64	34.6	51.9	Medical record	1	1	1	1

Lui 2009 <sup>65</sup>	Cohort	234	8	21.9	44.4	Medical record	1	1	1	1
Nyman and Jonsson 1986 <sup>66</sup>	Cohort	110	10	30.4 (s)	34.5	Medical record	1	1	1	1
Roos et al. 1992 <sup>67</sup>	Matched cc	66	33	34.5	30.3	Psychol. autopsy	2	2	?	1
Salama 1988 <sup>68</sup>	Cohort	139	5	?	39	Medical record	1	2	1	1
Stephens et al. 1999 <sup>69</sup>	Cohort	1212	28	28	52.6	Medical record	1	1	1	2
Taiminen et al. 2001 <sup>8</sup>	Matched cc	138	69	39.7	39.1	Psychol. autopsy	1	2	1	1
Wolfersdorf & Neher 2003 <sup>70</sup>	Matched cc	160	80	?	?	Medical record	1	1	1	1
<i>Mixed psychiatric</i>										
Brown et al. 2000 <sup>71</sup>	Cohort	6891	49	36.3	55.8	Interview part.	1	1	1	1
Bukstein et al. 1993 <sup>72</sup>	Matched cc	35	23	18.3	5.4	Interview NOK	1	2	1	2
Conlon et al. 2007 <sup>73</sup>	Matched nested cc	78	39	41.8	28.2	Medical record	1	1	1	?
Kjelsberg et al. 1991 <sup>74</sup>	Matched nested cc	42	21	33.5	42.9	Medical record	1	1	1	?
Kullgren 1988 <sup>75</sup>	Case control	14	8	34.1	0	Medical record	1	1	1	1
Kuo et al. 2011 <sup>76</sup>	Matched nested cc	114	38	28.9	18.4	Medical record	1	1	1	2
Murphy et al. 1992 <sup>77</sup>	Case control	315	67	45.1	0	Historical data	2	2	1	1
Simon et al. 2013 <sup>78</sup>	Cohort	84418	46	?	?	Interview part.	1	1	1	1
Thong et al. 2008 <sup>79</sup>	Matched cc	246	123	43 (s)	45.4	Medical record	1	1	1	2
<i>General population</i>										
Appleby et al. 1999 <sup>80</sup>	Matched cc	148	84	26.7	19	Psychol. autopsy	1	2	1	2
Castle et al. 2004 <sup>81</sup>	Case control	5624	1429	47.2	37	Interview NOK	2	2	1	2
De Leo et al. 2013 <sup>9</sup>	Case control	443	261	57.5	24.2	Interview NOK	2	2	1	2
Didham et al. 2006 <sup>82</sup>	Matched nested cc	884	221	med 37.2 (s)	25.8 (s)	Medical record	1	1	1	1
Jollant et al. 2014 <sup>10</sup>	Matched nested cc	45	15	30 (s)	47.7	Interview NOK	1	2	2	1

Table continued on the next page.



First author, year	Study design <sup>a</sup>	Sample size	Suicides	Age (years) <sup>b</sup>	% female	SI assessment <sup>c</sup>	Q1 <sup>d</sup>	Q2	Q3	Q4
Khang et al. 2010 <sup>83</sup>	Cohort	5414	13	>30	53.4	Interview part.	1	1	1	1
Kleiman and Liu 2014 <sup>84</sup>	Cohort	20014	25	47.6	53.1	Interview part.	1	1	1	1
Mock et al. 1996 <sup>85</sup>	Matched nested cc	84	21	21	20	Medical record	1	1	1	1
Palacio et al. 2007 <sup>86</sup>	Matched cc	216	108	med 29	19.4	Psychol. autopsy	2	2	1	1
Rowe et al. 2006 <sup>87</sup>	Case control	18	14	76.2	27.8	Psychol. autopsy	1	2	1	2
Zonda 2006 <sup>88</sup>	Matched cc	200	100	52.2	33	Interview NOK	2	2	1	1
<i>Various</i>										
Brinkman et al. 2014 <sup>89</sup>	Cohort	10072	10	25.0	49.7	Interview part.	1	1	1	1
Crandall et al. 2006 <sup>90</sup>	Cohort	218263	408	34.5	49.0	Medical record	1	1	1	1
Fruehwald et al. 2004 <sup>91</sup>	Matched nested cc	660	220	34.2	2.7	Medical record	1	1	1	2
Hyman 2012 <sup>92</sup>	Cohort	4045993	406	29.3	15.0	Military record	1	1	?	1
Mahon et al. 2005 <sup>93</sup>	Matched nested cc	126	63	29	0	Military record	2	1	1	1
McEwan et al. 2010 <sup>94</sup>	Cohort	138	3	36.4	10.9	Interview part.	1	1	1	1
McManus et al. 2014 <sup>95</sup>	Matched nested cc	81	17	41.3	0	Medical record	1	1	1	1
Thoresen & Mehlum 2004 <sup>96</sup>	Nested cc	88	43	30.5	0	Interview NOK	2	2	1	2

(s) denotes the value is only given for the suicide group; cc, case control; SI, suicidal ideation; Q, quality criterion; med, median; NOK, next of kin; part., participant; psychol., psychological; quest., questionnaire.

<sup>a</sup> If case control studies only did time matching (e.g. same admission date) we did not consider this a matched case control study.

<sup>b</sup> Mean age of study population is shown unless otherwise specified.

<sup>c</sup> Questionnaire clinician and interview next of kin were retrospective suicidal ideation assessment methods after the participant had reached study end point.

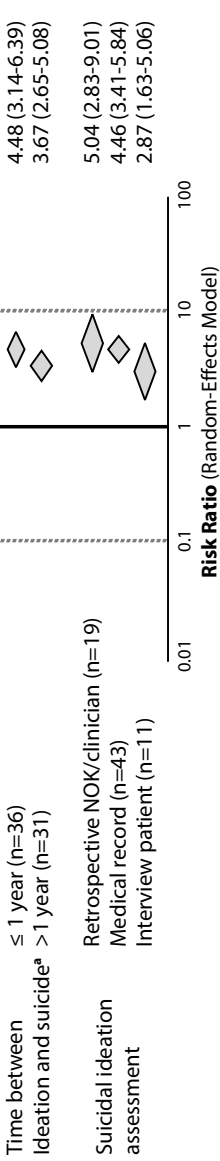
<sup>d</sup> Quality criteria, for specification see supplement S2.

<sup>e</sup> Study participants who attempted suicide were excluded before calculation of the effect size because it was unclear whether they had expressed suicidal ideation.

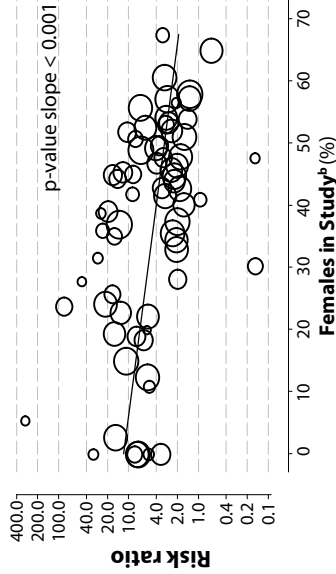
<sup>f</sup> Only data for male participants was used as the suicidal ideation effect size could only be calculated for males in this study.

**Supplement S4.** Subgroup analyses.

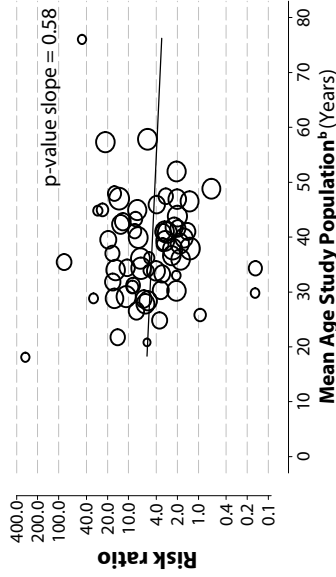
**A Subgroup analyses**



**B Meta-regression: effect of gender**



**C Meta-regression: effect of mean age**



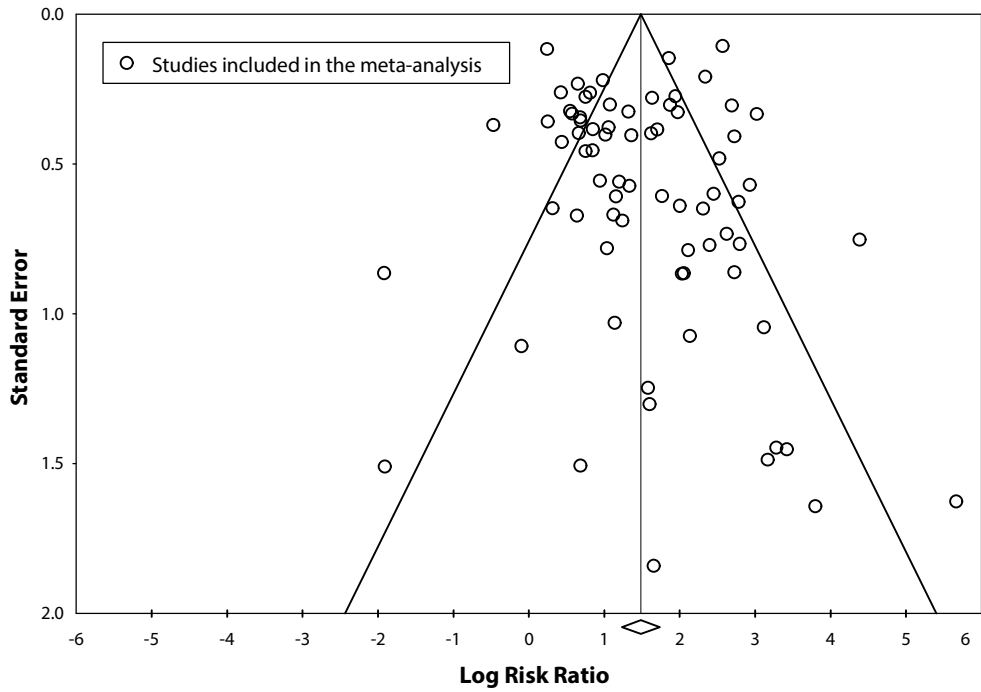
**Supplementary Figure 1.** Subgroup analyses.

Subgroup analyses showing the association between the expression of suicidal ideation and subsequent completed suicide in different subgroups. RR indicates risk ratio; CI, confidence interval; NOK, next of kin. B & C: Maximum likelihood meta-regression analysis with % of females in study (for B) and mean age of the study population (for C) as determinant and log<sub>e</sub>-transformed risk ratio as outcome presented on logarithmic scales. The bubble size is proportional to the study's weight.

<sup>a</sup> Total does not add up to 73, as in 8 studies the time interval could not be extracted and in 2 studies separate outcomes for ≤ and > 1 year were reported. When suicidal ideation was assessed at admission and suicide during admission, we assumed a time ≤ 1 year unless otherwise specified in the article.

<sup>b</sup> In 2 studies the % of females and in 8 studies the mean age of the study population was not provided.

**Supplement S5.** Publication bias



**Supplementary Figure 2.** Funnel plot displaying effect estimates from included studies. Egger's test for funnel plot asymmetry:  $p = 0.82$ .

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