

# Suicidal Ideation and Suicide Attempts After Direct or Indirect Psychotherapy A Systematic Review and Meta-Analysis

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# Suicidal Ideation and Suicide Attempts After Direct or Indirect Psychotherapy

## A Systematic Review and Meta-Analysis

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[+ Supplemental content](#)

**IMPORTANCE** Suicidal ideation and suicide attempts are debilitating mental health problems that are often treated with indirect psychotherapy (ie, psychotherapy that focuses on other mental health problems, such as depression or personality disorders). The effects of direct and indirect psychotherapy on suicidal ideation have not yet been examined in a meta-analysis, and several trials have been published since a previous meta-analysis examined the effect size of direct and indirect psychotherapy on suicide attempts.

**OBJECTIVE** To investigate the effect sizes of direct and indirect psychotherapy on suicidal ideation and the incidence of suicide attempts.

**DATA SOURCES** PubMed, Embase, PsycInfo, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials were searched for articles published up until April 1, 2023.

**STUDY SELECTION** Randomized clinical trials of psychotherapy for any mental health problem, delivered in any setting, compared with any control group, and reporting suicidal ideation or suicide attempts were included. Studies measuring suicidal ideation with 1 item were excluded.

**DATA EXTRACTION AND SYNTHESIS** PRISMA guidelines were followed. Summary data were extracted by 2 independent researchers and pooled using 3-level meta-analyses.

**MAIN OUTCOMES AND MEASURES** Hedges  $g$  was pooled for suicidal ideation and relative risk (RR) was pooled for suicide attempts.

**RESULTS** Of 15 006 studies identified, 147 comprising 193 comparisons and 11 001 participants were included. Direct and indirect psychotherapy conditions were associated with reduced suicidal ideation (direct:  $g$ ,  $-0.39$ ; 95% CI,  $-0.53$  to  $-0.24$ ;  $I^2$ , 83.2; indirect:  $g$ ,  $-0.30$ ; 95% CI,  $-0.42$  to  $-0.18$ ;  $I^2$ , 52.2). Direct and indirect psychotherapy conditions were also associated with reduced suicide attempts (direct: RR, 0.72; 95% CI, 0.62 to 0.84;  $I^2$ , 40.5; indirect: RR, 0.68; 95% CI, 0.48 to 0.95;  $I^2$ , 0). Sensitivity analyses largely confirmed these results.

**CONCLUSIONS AND RELEVANCE** Direct and indirect interventions had similar effect sizes for reducing suicidal ideation and suicide attempts. Suicide prevention strategies could make greater use of indirect treatments to provide effective interventions for people who would not likely seek treatment for suicidal ideation or self-harm.

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Suicide is the second leading cause of nonnatural death worldwide.<sup>1</sup> The number of people who attempt suicide is estimated to be more than 20 times higher than the number of people who die by suicide.<sup>2</sup> Suicide attempts, defined as acts in which a person harms himself or herself with the intention to die,<sup>3</sup> are associated with adverse long-term outcomes, including repeated suicide attempts, hospitalization, unemployment, and persistent mental health problems, such as suicidal ideation.<sup>4</sup> Suicidal ideation (ie, thinking about suicide with or without suicidal intent)<sup>3</sup> has a 12-month prevalence of 1% to 3% and lifetime prevalence of about 10% in the general population,<sup>5,6</sup> and a point prevalence of 20% in patient populations.<sup>7</sup> Suicidal ideation, in turn, is a major risk factor for suicide attempts and suicide.<sup>7</sup>

Psychotherapy has been found to reduce suicidal ideation and attempts.<sup>8,9</sup> Suicidal ideation, suicide attempts, and self-harm in general have traditionally been considered to be symptoms of other mental disorders, such as depressive disorders and borderline personality disorder.<sup>10,11</sup> As a result, health care systems tend to treat suicidal ideation and attempts in the context of other disorders, and many patients with suicidal ideation or suicide attempts receive indirect psychotherapy—that is, psychotherapy for mental health problems other than suicidal ideation or self-harm.<sup>12,13</sup>

Several types of psychotherapy have been developed that aim to reduce suicidal ideation or suicide attempts directly, such as dialectical behavior therapy,<sup>14</sup> Collaborative Assessment and Management of Suicidality,<sup>15</sup> or cognitive behavior therapy for suicide prevention.<sup>16</sup> The *DSM-5* introduced suicidal behavior disorder as a separate classification, which may pave the way for health systems and insurers to adapt these direct treatments.

A previous meta-analysis<sup>12</sup> showed effects of indirect treatment on the risk of suicide attempts at follow-up measurements (eg, 3 or 6 months after randomization) rather than immediately after treatment. Direct treatments also showed effects on suicide attempts immediately after treatment.<sup>12</sup> Another meta-analysis<sup>8</sup> found that self-harm treatments led to similar reductions in suicidal ideation compared with indirect treatments. Both meta-analyses included treatments other than psychotherapy (eg, outreach, case management, and pharmacotherapy), so no conclusions can be drawn about the effect of direct or indirect psychotherapy. In addition, many studies reporting the effect of psychotherapy on suicidal ideation and suicide attempts have been published since the authors of these meta-analyses searched the literature. The present study is a systematic review and meta-analysis of the effect of psychotherapy on suicidal ideation and suicide attempts, distinguishing between psychosocial interventions that directly target suicidal ideation or suicide attempts and psychotherapeutic interventions that target other mental health problems.

## Methods

The current study is part of a larger living systematic review that examines the effect of psychotherapy on suicide-related outcomes.<sup>17,18</sup> The extracted data and documentation are

### Key Points

**Question** What are the effects of suicide-focused (direct) and other (indirect) psychotherapies on suicidal ideation and suicide attempts?

**Findings** In this systematic review and meta-analysis of 147 studies comprising 193 comparisons and 11 001 participants, direct and indirect interventions were associated with significant reductions in suicidal ideation and suicide attempts.

**Meaning** The findings suggest that both direct and indirect psychotherapies can be used to reduce the severity of suicidal ideation and risk of suicide attempts.

online.<sup>19,20</sup> For the present article, we followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guideline.<sup>21</sup>

### Identification and Selection of Trials

The full search strings can be found in eAppendix 2 in [Supplement 1](#). A systematic search of articles published up to April 1, 2023, was run in PubMed, Embase, PsycInfo, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials.

Studies were included if they met the following criteria: (1) had a randomized design comparing 2 or more groups; (2) examined psychotherapy (the use of psychological methods to change behavior or overcome problems) targeting any mental health problem and delivered in any setting (including guided digital treatments); (3) compared the intervention with a control group (such as care as usual, enhanced care as usual, or waiting list); (4) reported suicidal ideation (SI), suicide attempts (SA), or self-harm leading to hospitalization (only included if the authors' definition of self-harm included suicide attempts). Studies were excluded if they (1) used an intervention that did not involve any psychotherapeutic technique or support (eg, unguided self-help and community intervention) and (2) measured SI on a categorical scale, such as a single item of a questionnaire for depression. We included studies on all age groups. All abstracts and full texts were screened by 2 independent researchers, and conflicts were discussed with a third researcher.

### Data Extraction

Data were extracted by 2 independent researchers. Disagreements were solved by discussion and, if necessary, in consultation with a third researcher. We coded treatments as direct if part or all of the treatment was aimed at influencing SI or if part or all of the treatment was aimed at preventing suicide attempts. Interventions that targeted self-harm according to the definition commonly used in the UK were also considered direct because, according to this definition, self-harm can include suicide attempts. Treatments were coded as indirect when no part was explicitly aimed at suicidal ideation, suicide attempts, or self-harm. As our focus was on between-group effects, we only considered those components of the intervention that were not also part of the control condition. Interrater agreement on this direct or indirect coding was 75% for the first 20 studies and 95% for the last 20 studies. In case

of doubt or discrepancies, a third researcher (R.d.W.), a psychiatrist specializing in suicide prevention treatments, was consulted.

We extracted participant characteristics (eg, proportion of women, mean age, and disorder), characteristics of the psychological treatments (eg, type of therapy and treatment format), assessment characteristics (eg, type of outcome measure used), and characteristics of the studies (eg, setting, type of control group, and country).

### Risk of Bias

Risk of bias was assessed by 2 independent reviewers using the Cochrane risk of bias 2 (RoB 2) assessment tool. The risk of bias 2 tool assesses possible sources of bias in randomized clinical trials arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, or selection of the reported result.

### Outcome Measures

We extracted posttreatment SI severity, usually reported as means and standard deviations on a self-report scale or clinical interview, and the number of people who attempted suicide between the baseline and posttreatment assessments. Posttreatment was defined as the first assessment after participants had completed the treatment protocol. In trials where self-harm could include suicide attempts but suicide attempts were not reported separately, we counted the number of people who were hospitalized after an episode of self-harm. People who died by suicide were also considered to have attempted suicide. We did not estimate effect sizes for suicide alone, as these events are rare.

For SI, we calculated the effect size indicating the difference in SI severity between the 2 groups at posttest (Hedges  $g$ ) for each comparison between a psychological treatment and a control condition. When the means and standard deviations were not reported in the article, we extracted change scores from baseline to posttest or binary outcomes (eg, proportion of participants who responded or remitted) or any other statistic (such as  $P$  value or  $t$  value). Whenever possible, we prioritized intention-to-treat outcomes. For SA, we calculated the relative risk (RR) as the proportion of people who attempted suicide in the psychotherapy group divided by the proportion in the control group.

### Meta-Analyses

We conducted 4 separate meta-analyses: 1 for each outcome (ie, SI and SA) and 1 for each intervention type (ie, direct and indirect treatments). Data were analyzed with the `metapsyTools` package in R version 4.1.3 and RStudio (R Foundation) (also see the eMethods in [Supplement 1](#)). We estimated 3-level models with effect sizes nested in studies to account for multiarm trials, applying robust variance estimation, assuming correlated hierarchical effects<sup>22</sup> (also see the eMethods in [Supplement 1](#)). We assumed an intrastudy correlation of  $\rho = 0.6$ . Relative risk was pooled using Mantel-Haenszel methods, which give appropriate estimates of standard errors when there are few events.

We calculated the  $I^2$  statistic and its 95% CI, which is an indicator of heterogeneity in percentages. A value of 0% indicates no observed heterogeneity, and larger values indicate increasing heterogeneity, with 25% indicating low, 50% moderate, and 75% high.<sup>23</sup> Considering we had 3-level models, we calculated a multilevel extension of  $I^2$ , which describes the amount of total variability attributable to heterogeneity within studies (level 2) and heterogeneity between studies (level 3).<sup>24,25</sup> We also added the prediction interval, which indicates the range in which the true effect size of 95% of all populations will fall.<sup>26,27</sup> Between-study heterogeneity variance (components), denoted by  $\tau^2$ , were estimated using restricted maximum likelihood. Next, we tested the robustness of the outcomes by (1) excluding outliers, defined as when the 95% CI of the effect size does not overlap with the 95% CI of the pooled effect size<sup>25</sup>; (2) excluding influential cases, according to the methods developed by Viechtbauer and Cheung<sup>28</sup>; (3) adjusting for publication bias, using the limit meta-analysis method<sup>29</sup> (eMethods in [Supplement 1](#)); (4) excluding studies that had a waiting list control group; and (5) calculating the pooled effect size with studies at low risk of bias.

Subgroup analyses were conducted for the following variables: country (US, Europe, Canada, Australia, and New Zealand vs other), SI as main complaint (also when SI was the main problem in combination with a clinical diagnosis), disorder as specified by the *DSM* versions III, IV, IV-TR, 5, and 5-TR or *International Classification of Diseases (ICD)* versions 9, 10, and 11, type of psychotherapy, and age group. We reported outcomes of subgroups when they consisted of 3 or more studies. We maintained a significance level of  $P < .05$ .

## Results

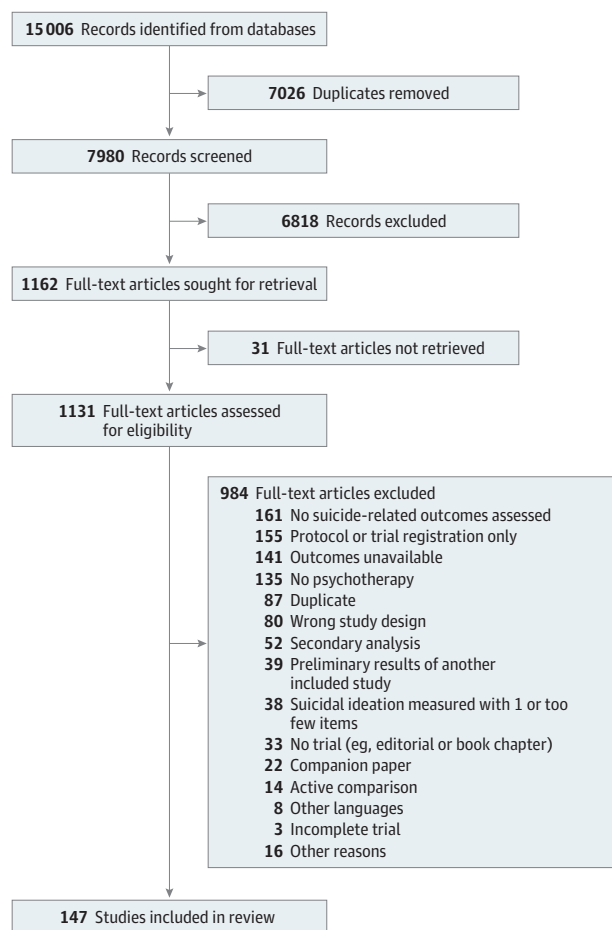
### Selection and Inclusion of Studies

We examined 15 006 records (7980 after removal of duplicates) and retrieved 1162 full-text articles. Ultimately, we included 147 studies comprising 193 comparisons, 103 of which investigated the effect of psychotherapy on SI severity and 90 of which investigated the effect of psychotherapy on SA or self-harm leading to hospitalization. The PRISMA flowchart is presented in the [Figure](#).

### Characteristics of Included Studies

Key characteristics of the included studies are presented in [Table 1](#) and in eTable 1 in [Supplement 1](#), with all included studies listed in the eReferences in [Supplement 1](#). Of the 103 psychotherapy conditions where SI was measured as an outcome, 64 (62%) directly targeted suicidal thoughts or attempts and 39 (38%) targeted other mental health problems. Of the 90 psychotherapy conditions where SA or self-harm leading to hospitalization was measured as an outcome, 64 (71%) were directly targeting suicidal thoughts or attempts and 26 (29%) other mental health problems. SI was measured among 9812 participants in total. SA or self-harm leading to hospitalization was measured among 14 443 participants, 1905 of whom (13.2%) attempted suicide. Participants in direct and indirect conditions reported similar levels of SI severity at baseline,

Figure. PRISMA Flow Diagram



based on studies using the Beck Scale for Suicidal Ideation (mean, 16.1 in studies on direct treatment and 15.7 in studies on indirect treatment), reflecting similar exclusion criteria for suicidal ideation or suicide risk between included studies of direct and indirect interventions.

Regarding psychotherapy, 27% of direct conditions were cognitive behavioral therapy and 29% of indirect conditions were cognitive behavioral therapy. Other frequent conditions were family therapy (10%), psychodynamic treatment (6%), and dialectical behavior therapy (6%). In nearly all trials, participants in the intervention and control conditions used psychotropic medication. The most common control conditions were care as usual and enhanced care as usual (71% of control conditions). Care as usual conditions usually consisted of regular contact with a psychiatrist to monitor medication. Enhanced care as usual comprised care as usual and an additional element, such as a single group session or monthly telephone calls. Indirect interventions were compared with waiting list control in 24% of comparisons, while direct interventions were compared with waiting list control in 5% of comparisons.

Most studies were rated as high risk of bias (eFigures 1 and 2 in Supplement 1). Studies rated as low risk or some con-

Table 1. Selected Study Characteristics

	Treatments, No. (%)	
	Direct	Indirect
<b>Suicidal ideation</b>		
Comparisons, No.	64	39
Participants, No.	6606	3206
Women	4769 (72.2)	1394 (43.5)
Men	1837 (27.8)	1812 (56.5)
Mean age, y	27.9	24.2
Inpatients	1268 (19.2)	269 (8.4)
Suicidal ideation or self-harm was primary mental health problem	6163 (93.3)	1003 (31.3)
Mean suicidal ideation severity at baseline (studies using the Beck Scale for Suicidal Ideation only)	16.1	15.7
<b>Suicide attempts</b>		
Comparisons, No.	64	26
Participants, No.	11 535	2908
Women	7994 (69.3)	1533 (52.7)
Men	3541 (30.7)	1375 (47.3)
Mean age, y	26.2	25.3
Inpatients	1004 (8.7)	0
Suicidal ideation or self-harm was primary mental health problem	1127 (95.6)	648 (22.3)
Participants who attempted suicide between baseline and posttreatment assessment	1615 (14.0)	290 (10.0)

cerns were 8% (8 of 103) of those measuring SI and 19% (17 of 90) of those measuring SA. Because of these proportions, we based the risk of bias sensitivity analysis on domain 3 (missing outcome data) only.

### Effect Sizes of Direct and Indirect Interventions for Suicidal Ideation and Attempts

The results of the main analyses are reported in Table 2 and eTable 2 in Supplement 1. Direct and indirect psychotherapy conditions were associated with reduced SI (direct:  $g$ ,  $-0.39$ ; 95% CI,  $-0.53$  to  $-0.24$ ; indirect:  $g$ ,  $-0.30$ ; 95% CI,  $-0.42$  to  $-0.18$ ). Heterogeneity was high among studies on direct interventions and moderate among studies on indirect interventions. Direct and indirect psychotherapy conditions were also associated with reduced SA (direct: RR, 0.72; 95% CI, 0.62 to 0.84; indirect: RR, 0.68; 95% CI, 0.48 to 0.95). Heterogeneity among studies measuring SA was low (Table 2).

Sensitivity analyses are also shown in Table 2 and eTable 2 in Supplement 1. There were few outliers detected, except among studies on direct psychotherapy measuring SI (8 outliers removed; adjusted  $g$ ,  $-0.26$ ; 95% CI,  $-0.34$  to  $-0.18$ ). Removing influential cases or removing studies with waiting list control conditions hardly affected the results. Adjusting for publication bias had an impact on the pooled effect size of indirect psychotherapy on SI and on the pooled effect size of direct psychotherapy on SA, both of which were no longer significant. Analyses restricted to studies rated as low risk for bias missing outcome data were similar to the main analyses. The pooled effect size of indirect psychotherapy on SA was robust and remained similar and statistically significant in all sensitivity analyses.



Table 2. Summary of Main Analyses and Sensitivity Analyses

Treatment type	Suicidal ideation			Suicide attempts		
	Comparisons, No.	Pooled effect, Hedges <i>g</i> (95% CI)	<i>I</i> <sup>2</sup>	Comparisons, No.	Pooled effect, relative risk (95% CI)	<i>I</i> <sup>2</sup>
<b>Direct</b>						
3-Level meta-analysis	64	−0.39 (−0.53 to −0.24) <sup>a</sup>	83.2	64	0.72 (0.62 to 0.84) <sup>a</sup>	40.5
Outliers removed	56	−0.26 (−0.34 to −0.18) <sup>a</sup>	38.1	60	0.71 (0.62 to 0.81) <sup>a</sup>	16.2
Influential cases removed	61	−0.25 (−0.35 to −0.16) <sup>a</sup>	54.8	60	0.68 (0.58 to 0.79) <sup>a</sup>	23.3
Adjusted for publication bias	64	−0.18 (−0.32 to −0.04) <sup>a</sup>	95.8	64	0.94 (0.82 to 1.09)	98.1
Low risk of bias due to missing outcome data	27	−0.50 (−0.84 to −0.16) <sup>a</sup>	84.6	32	0.68 (0.54 to 0.85) <sup>a</sup>	50.1
Waiting list conditions removed	59	−0.36 (−0.50 to −0.21) <sup>a</sup>	81.8	64	0.72 (0.62 to 0.84) <sup>a</sup>	40.5
<b>Indirect</b>						
3-Level meta-analysis	39	−0.30 (−0.42 to −0.18) <sup>a</sup>	52.2	26	0.68 (0.48 to 0.95) <sup>a</sup>	0
Outliers removed	37	−0.23 (−0.33 to −0.13) <sup>a</sup>	27.4	26	0.68 (0.48 to 0.95) <sup>a</sup>	0
Influential cases removed	38	−0.25 (−0.37 to −0.14) <sup>a</sup>	40.0	24	0.71 (0.50 to 0.99) <sup>a</sup>	0
Adjusted for publication bias	39	−0.16 (−0.34 to 0.03)	92.6	26	0.66 (0.48 to 0.90) <sup>a</sup>	0
Low risk of bias due to missing outcome data	18	−0.29 (−0.49 to −0.09) <sup>a</sup>	55.6	13	0.71 (0.56 to 0.91) <sup>a</sup>	0
Waiting list conditions removed	25	−0.30 (−0.45 to −0.15) <sup>a</sup>	58.3	26	0.68 (0.48 to 0.95) <sup>a</sup>	0

<sup>a</sup> Statistically significant (*P* < .05).

### Subgroup Analyses

Several significant differences in effect sizes were found in subgroup analyses (eTable 2 in Supplement 1). Among direct treatments, Collaborative Assessment and Management of Suicidality (*g*, −0.46; 95% CI, −0.85 to −0.08) and cognitive behavioral therapy (*g*, −0.51; 95% CI, −0.91 to −0.12) had significantly larger effect sizes on SI than psychodynamic-oriented therapy (*g*, 0.01; 95% CI, −0.36 to 0.39) (*P* = .03). Dialectical behavior therapy (RR, 0.49; 95% CI, 0.39 to 0.60) and cognitive behavioral therapy (RR, 0.65; 95% CI, 0.50 to 0.83) had significantly larger effect sizes on SA than Collaborative Assessment and Management of Suicidality (RR, 1.14; 95% CI, 0.34 to 3.81), family therapy (RR, 1.14; 95% CI, 0.87 to 1.49), and problem-solving therapy (RR, 0.99; 95% CI, 0.77 to 1.29) (*P* < .001). Subgroup analyses were limited because of low numbers and high heterogeneity.

### Discussion

This systematic review and meta-analysis found that psychosocial interventions were associated with significant reductions in the severity of suicidal ideation and the incidence of suicide attempts. The observed results were similar for direct interventions—that is, those specifically targeting suicidal ideation or suicide attempts—and for indirect interventions targeting other mental health problems. Although the pooled effect size for suicidal ideation was small,<sup>30</sup> the 30% lower risk of suicide attempts associated with both direct and indirect treatments can be considered clinically relevant, given the severity of such events.

Even though the pooled effect sizes of direct and indirect treatments were similar, caution is warranted. Direct and indirect interventions have not been compared head to head in 1 trial, and the trials in both groups were heterogeneous in terms of in-

tervention format and length, type of control condition, and outcome measures. Baseline suicidal ideation severity was similar in both study groups, but there were differences in population characteristics between trials on direct and indirect treatments. There were also signs of publication bias, particularly for the effect of direct treatment on suicide attempts.

Most patients in direct conditions had suicidal ideation or self-harm as their primary mental health problem, and most patients in indirect conditions had other primary disorders. This reflects clinical practice, where treatments are usually tailored to the problem for which patients are seeking treatment. Our findings suggest that this may be good practice, even when patients have severe suicidal ideation and are seeking help for another mental health problem. Indirect effects may be explained by a decrease in the severity of suicidal ideation as a patient's overall mental health improves, or by patients applying techniques learned in therapy (eg, cognitive behavioral therapy for depression) to their suicidal thoughts.

Suicide prevention strategies could make use of indirect effects. The average proportion of individuals with past-year suicide ideation, plans, or attempts seeking or engaging with mental health services is estimated to be around 30%,<sup>31</sup> and perceived stigma is one of the reasons for this low percentage. As has been suggested for depression,<sup>32</sup> treatments targeting less stigmatizing problems may be a way to provide effective interventions to people who would not likely seek treatment for suicidal ideation or self-harm. On the other hand, direct interventions may have additional merit for health care professionals, because they could provide tangible tools and strategies and enhance clinicians' confidence when dealing with suicidal ideation and attempts.

The findings of our study indicate that many different treatments are available and that it is possible that certain patient groups would benefit from a specific treatment, for example in terms of content, format, duration, and health care profes-

sional. It has been argued that personalized treatment could increase the effectiveness and efficiency of mental health care in general.<sup>33</sup> Some of these research questions can be answered with the data collected for this meta-analysis. In addition, which treatment works best for whom can be investigated by an individual patient data meta-analysis.<sup>17</sup>

A previous meta-analysis by Meerwijk et al<sup>12</sup> on the relationship between direct and indirect interventions and suicide attempts found that only direct interventions were associated with reducing suicide attempts posttreatment, while significant effect sizes for both types of treatment were found at longer follow-up. We found that both direct and indirect interventions were associated with reducing suicide attempts posttreatment, likely due to increased statistical power from the large number of studies published since 2016 (88 comparisons compared with 31 in Meerwijk et al).

### Limitations

This meta-analysis has limitations. First, our definition of direct treatment is relatively inclusive, and therefore the group of studies on direct treatment was heterogeneous. Second, even though our definition of indirect treatment was stringent, we cannot know whether suicidal ideation was never discussed between clinicians and patients in indirect conditions. There were studies on indirect treatments that explicitly recruited patients with suicidal ideation or a history of sui-

cide attempts. Third, most studies were on young adults or adults, so our results may be less representative for other age groups. Fourth, we focused on posttreatment outcomes and did not include follow-up measurements. We decided not to include these because posttreatment measurement is most indicative of immediate treatment effect and patient safety, and because the moment of follow-up differed substantially between studies (2 to 24 months after baseline). Fifth, we could not fully adjust for demographic or diagnostic differences between the samples due to insufficient data. The best way to analyze this would be a meta-analysis of individual patient data.

### Conclusions

In this study, psychosocial interventions were associated with significant reductions in the severity of suicidal ideation severity and the incidence of suicide attempts. The observed effect sizes were similar for direct interventions (ie, those specifically targeting suicidal thoughts or suicide attempts) and indirect interventions (ie, those targeting other mental health problems). Suicide prevention strategies could make more use of indirect treatments as a strategy to get effective interventions to people who would not be likely to seek treatment for suicidal ideation or self-harm.

#### ARTICLE INFORMATION

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**Acquisition, analysis, or interpretation of data:** van Ballegooijen, Rawee, Palantza, Miguel, Harrer, Cristea, Eikelenboom, Cuijpers.

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**Supervision:** van Ballegooijen, Cristea, de Winter, Beekman.

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