
Article:
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Manuscript Details

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Title	Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis
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Abstract

Objective: This study provides an estimate of the effect size of suicide prevention interventions and evaluates the possible synergistic effects of multilevel interventions. Method: A systematic review and meta-analysis were conducted of controlled studies evaluating suicide prevention interventions versus control published between 2011–2017 in PubMed, PsycINFO, and Cochrane databases. Data extraction and risk of bias assessment according to ROBINS criteria were performed by independent assessors. Cohen's delta was calculated by a random meta-analysis on completed and attempted suicides as outcomes. Meta-regression explored a possible synergistic effect in multilevel interventions. PROSPERO ID number: X. Results: The search yielded 16 controlled studies with a total of 252,932 participants. The meta-analysis was performed in 15 studies with 29,071 participants. A significant effect was found for suicide prevention interventions on completed suicides (d=-0.535, 95% CI -0.898; -0.171, p=.004) and on suicide attempts (d=-0.449, 95% CI -0.618; -0.280, p<.001). Regarding the synergistic effect of multilevel interventions, meta-regression showed a significantly higher effect related to the number of levels of the intervention (p=.032). Conclusions: Suicide prevention interventions are effective in preventing completed and attempted suicides and should be widely implemented. Further research should focus on multilevel interventions due to their greater effects and synergistic potential. Further research is also needed into risk appraisal for completed versus attempted suicide, as the preferred intervention strategy differs with regard to both outcomes.

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Submission Files Included in this PDF

File Name [File Type]

Cover letter Effectiveness of Suicide Prevention Interventions.docx [Cover Letter]

Response to reviewers.docx [Response to Reviewers (without Author Details)]

Revised blinded manuscript Effectiveness Suicide Prevention Interventions.docx [Revised Manuscript with Changes Marked (without Author Details)]

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Figure 1. PRISMA flow diagram (2009).pdf [Figure]

Figure 5. Meta-regression of number of intervention-levels.pdf [Figure]

Figure 6. Funnel plot.pdf [Figure]

Submission Files Not Included in this PDF

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Figure 2. Forest plot suicidal behavior.xlsx [Figure]

Figure 3. Forest plot completed suicides.xlsx [Figure]

Figure 4. Forest plot attempted suicides.xlsx [Figure]

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Editor
General Hospital Psychiatry

Dear editor,

Hereby we would like to submit the manuscript 'Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis' by the following authors Emma Hofstra, Chijs van Nieuwenhuizen, Marjan Bakker, Dilana Özgül, Iman Elfeddali, Sjakko J. de Jong and Christina M. van der Feltz-Cornelis. We hope that you will consider publication in General Hospital Psychiatry.

The aim of the study was to examine the effectiveness of suicide prevention interventions in terms of completed and attempted suicides, and to provide an estimate of their effect size. Furthermore, to study whether effectiveness differs across settings in which the intervention is delivered and to explore synergism in multilevel interventions. This was done by means of systematic review and meta-analysis on controlled studies evaluating suicide prevention interventions versus controls that were published between 2011-2017 in PubMed, PsycINFO and Cochrane databases. In this study we found a significant effect for suicide prevention interventions on completed suicides and on suicide attempts. Also, meta-regression showed a significantly higher effect in relation to the number of intervention-levels on its effectiveness. This systematic review and meta-analysis targets important gaps in Suicidology as this is – as far as we know - the very first systematic review and meta-analysis that provides an estimate of the effect of suicide prevention interventions on completed and attempted suicides in controlled studies. Also, it is the first study that explores synergism of multilevel interventions in a quantitative manner.

This research was funded by The Netherlands Organisation for Health Research and Development, grant number 537001002. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors of this study had full access to all the data in the study and had final responsibility for the integrity of the data, the accuracy of the data analysis and the decision to submit for publication and all authors gave their agreement and approval for all aspects of the final version of the paper. The authors declare no competing interests.

Our manuscript has been professionally proofread by Proof Reading Services (PRS).

In case our manuscript is too long for publication as a whole, we would like to discuss with you the possibilities to publish a shortened version. For example, to shorten our manuscript, certain sections in the Methods section as well as certain figures might also be published as online supplements.

We thank you in advance for reviewing our manuscript and for considering it for publication.

This manuscript is not previously published elsewhere or under consideration by another journal.

Kind regards, also on behalf of the co-authors,

Emma Hofstra

Ref: GHP_2018_474
Title: Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis
Journal: General Hospital Psychiatry

Dear dr. Huffman,

We have received the review of our manuscript submitted to General Hospital Psychiatry and we would like to thank you for inviting us to resubmit it. The reviewers' feedback helped us to strengthen the manuscript. In this revision letter, we will reply to the reviewers' comments and outline the changes we have made in our manuscript. We will also submit a revised version of the manuscript.

Reviewer 1

This manuscript presents the findings from a systematic review and meta-analysis of effectiveness of interventions aimed to prevent suicidal behavior. Though a relatively large number of recent systematic and non-systematic reviews exist, the authors state that their work is the first attempt to generate an effect size of studies testing suicide prevention interventions (against a control condition). Strengths of the study include the clear and concise writing style, structured and systematized literature search, coding process, and reporting of results in line with existing standards (e.g., PRISMA), large N across studies (> 250,000 participants total), analyses appropriate to the data at hand, clear presentation of results overall (though see minor points below about figures), and examination of relevant moderating variables. I believe this is a strong review that will contribute nicely to the existing literature - I was surprised to learn that no review to date has generated an effect size of suicide prevention interventions in controlled studies - and has the potential to be highly cited. I do have a number of suggestions (mostly minor and all addressable, I believe) to improve this study's potential to contribute in a meaningful way to the field's knowledge about effectiveness of suicide-focused interventions.

R: We would like to thank the reviewer for his/her compliments as well as for the suggestions made. We hope to have met the reviewers' comments by the adjustments made in our revised manuscript.

First, the authors place notable emphasis on their examination of the "synergistic effects" of multilevel interventions, despite the fact that only two studies testing multilevel interventions were included. Though this is very briefly noted as a limitation in the Discussion section, I suggest the authors significantly temper their discussion of the implications of their findings specific to multilevel interventions as there was only one two-level intervention and one three-level intervention. This includes tempering the degree to which these findings are emphasized, particularly in the Abstract (e.g., "Multilevel interventions should be the strategy of choice due to a greater effect and a synergistic potential") and Discussion (e.g., "multilevel interventions are more effective than single level interventions…" page 25). In this part of the Results section, the authors might remind the reader (as it is only mentioned much earlier on in the Methods) that there were two multi-level studies total. Though intuitively, multilevel interventions may be more promising for reducing suicidal behavior than one-level interventions, interpreting the present data from only two multilevel studies to "recommend the implementation of multilevel suicide prevention interventions above one level" may be premature, or at least a statement that should be tempered to reflect the small n of these types of studies.

R: We thank the reviewer for the recommendations regarding the findings specific to multilevel interventions. We therefore tempered our findings about multilevel interventions in the Abstract. We also reminded the reader that there were two multi-level studies in total in the Results section and tempered the implications of our findings in the Discussion.

We changed the following in the Abstract:

- *Page 1: Further research should focus on multilevel interventions due to their greater effects and synergistic potential.*

We added the following to the Results section:

- *Page 10, paragraph 'Study characteristics': A total of 16 studies were included in the systematic review. Of these studies, 14 examined a unilevel suicide prevention intervention and two a multi-level intervention. Of the two multi-level interventions, one study included completed suicides as an outcome measure and one study attempted suicides.*

We added the following to the Discussion:

- *Page 27, paragraph 'Strengths and Limitations' after 'A second limitation is that we only included two multilevel interventions in the meta-analysis' of which one was a two-level intervention and one was a three-level intervention. Multilevel interventions should, therefore, be the focus of further research, as the current evidence indicates a greater effect of multilevel interventions compared to unilevel interventions and synergistic potential.*
- *Page 29, paragraph 'Conclusion' Moreover, multilevel interventions should be the focus of further research due to a greater effect and synergistic potential.*

Second, the authors do not address the possibility that the number of occurrences of suicide attempts versus completed suicides (presumably, a much smaller number of observed completed suicides) may have impacted their differential findings for attempts on completed suicides (a key point in their Discussion). Do the authors have any thoughts about whether this might be another possibility (and if so, how this would impact results for effect sizes for suicide attempts versus deaths)?

R: A total of 15 studies were included in the meta-analysis, all together reporting 62 suicides and 1006 suicide attempts (participants might have attempted suicide multiple times). We added to the Discussion that more studies on completed suicide would foster making more precise estimates of the effects.

We added the following to the Discussion:

- *Page 27, paragraph 'Strengths and Limitations': Moreover, completed suicides remain a low base rate behavior. This resulted in our study in a less precise estimate of the effect, compared to suicide attempts. It is desirable for future research that more studies will examine the effect of suicide prevention interventions on preventing completed suicide, as more studies will enable more precise estimates of the effects.*

It might also be a useful piece of information, if possible, to include the total number of suicide deaths and attempts that were observed across the studies included (both to provide more context and possibly to further emphasize the value of the current review, in that a very large number of patients were included which resulted in a significant, notable number of suicide death occurrences, despite this being a very low base rate behavior).

R: We added the total number of suicide deaths and attempts in the Results section. We also included in the Discussion that a very large number of patients were included which resulted in a significant, notable number of suicide death occurrences, despite this being a very low base rate behaviour.

We added the following to the Results section:

- *Page 19, paragraph 'Synthesis of results': A total of 15 studies were included in the meta-analysis, all together reporting 62 suicides and 1006 suicide attempts (participants might have attempted suicide multiple times).*

We added the following to the Discussion:

- *Page 27, paragraph 'Strengths and Limitations': Moreover, despite completed suicides being a very low base rate behavior, we found significant results which is probably due to the very large number of patients that were included in our study.*

I also have a number of more minor suggestions/concerns:

1) Introduction – rationale: Suicide attempts are among the most important known predictors of suicide, not necessarily the most important predictor. It would also be helpful to include a citation specifically to support this point (e.g., Ribeiro et al 2016 meta-analysis from Psychological Medicine on prior suicidal behavior predicting suicide ideation, attempts, and deaths).

R: We thank the reviewer for the suggestion to include a citation to support the point about suicide attempts and we added the citation of Ribeiro et al. 2016.

We added the following to the Introduction:

- *Page 2: Suicide attempts are among the most important known predictors of completed suicide (Ribeiro et al., 2016).*

2) I encourage the authors to consider using the term "suicidal thoughts and behaviors" rather than suicidality as it is more specific/concrete and operationalized.

R: We have changed the term 'suicidality' into 'suicidal thoughts and behaviours' in the Introduction and Discussion, as recommended by the reviewer.

3) Objectives - #2: To explore if the setting of an intervention moderates efficacy (rather than "is associated with different effect sizes") – would this be appropriate to say? It is more consistent, I believe, with how such aims/analyses are usually described/reported in meta-analyses.

R: In our opinion, we did explore the association with setting and not a moderation. Moreover, other factors might be involved (for example as moderators) as well. Therefore, we would like to keep with the original formulation of this objective.

4) Eligibility criteria: The use of "should" throughout does not read well in this section, in my opinion; I would encourage the authors to use past tense (e.g., "eligible studies reported on…").

R: We changed this paragraph to the use of past tense.

We changed the following to the Methods section:

- *Page 4, paragraph Eligibility criteria: Studies were considered eligible if suicides and/or suicide attempts were included as an outcome and if a suicide prevention intervention was compared with a control group or period.*

5) Eligibility criteria: Please define "self-harm" (SH) – suicidal thoughts and behaviors? Suicidal and nonsuicidal thoughts and behaviors (e.g., nonsuicidal self-injury included as well)?

R: We added a definition of self-harm 'non-suicidal self-injury) in the manuscript.

We changed the following to the Methods section:

- *Page 4, paragraph Eligibility criteria: The exclusion criterion was the inclusion of self-harm (non-suicidal self-injury; SH) in the target group for the intervention.*

6) Study selection/data collection process: Did the authors calculate interrater reliability kappa coefficients? Or % of interrater agreement? If not, this might be noted as a limitation.

R: We thank the reviewer for this suggestion. However, the selection procedure in our study was not set up in a manner that calculating an interrater reliability kappa coefficient would be relevant. Therefore, we did not calculate interrater reliability kappa coefficients. Since it was not relevant for the procedure at hand, we do not consider this as a limitation of the study. For further clarification, we have described our procedure of risk of bias assessment in more detail.

7) Discussion: I am curious about the research to support the statements that individuals who complete suicide have fewer psychiatric problems than those who attempt suicide – could this be an artefact of those who complete suicide being less likely to see mental health practitioners? How strong are the studies to support this comment (given that it seems somewhat counterintuitive)?

R: We agree with the reviewer that more research is needed to whether individuals that complete versus attempt suicide differ in how many psychiatric disorders they have. Therefore, we changed this statement in the Discussion.

We changed the following to the Discussion:

- *Page 25: More research is needed to whether individuals that complete versus attempt suicide differ with regards the presence of psychiatric disorders.*

8) PRISMA figure: The "Records excluded (n=1)" box (presumably the Pearson et al. 2017 study) should include a brief mention of why that study was excluded (as described in more detail elsewhere in the paper).

R: We added a brief mention in the PRISMA figure of why the study of Person et al. 2017 was excluded.

We added the following in Figure 1:

- *Could not be pooled due to different outcomes (n = 1)*

9) The tables corresponding to the forest plots exported directly from CMA are somewhat blurry (at least in my version of the manuscript) and a bit hard to read. I would encourage the authors to consider putting the tabular information into a separate table (i.e., in word or excel), not export directly from CMA.

R: We created new forest plots -including the tables- in excel, to avoid blurriness.

Reviewer 2

Please clarify what the author's are referring to when they state "until now an estimate of the effect size has not been provided." Was the Odds Ratios in Zalsman et al. in 2016 not an effect size?

R: We would first like to thank the reviewer for the very attentive reading of our manuscript. We hope that the adjustments we made in the manuscript will meet the comments of the reviewer. With regards to the comment about an estimate of the effect size: the Odds Ratio in Zalsman et al. 2016 is indeed an effect size. However, it is based on one intervention in a school setting and a comparative estimate for the effect of different types of interventions has therefore not yet been provided. Therefore, we changed our statement in the Introduction and Discussion.

We changed the following in the Introduction:

- *Page 2: Despite growing evidence for the effectiveness of several suicide prevention strategies, until now a comparative estimate for the effect of different types of interventions has not yet been provided.*

We changed the following in the Discussion:

- *Page 24: The meta-analysis, for the first time, provides a comparative estimate for the effect of different types of suicide prevention interventions, based on 15 controlled studies, with 29,071 participants in various settings.*

Why limit studies to such a short window 2011-2017? If an effect size has not been reported then why not pool all available data? The systematic review of van der Feltz-Cornelis does not appear to have a reference where it is mentioned, pg. 5.

R: Our study further elaborates on the systematic review of van der Feltz-Cornelis, which was published in 2011. We extended our search from January 2011 through December 2017. For clarification of the reader, we added a reference on page 5 where we mentioned the time window of our study.

The outcomes are very poorly defined. Please elaborate and provide detailed information, e.g. was family report of an attempt eligible? This is particularly necessary to clarify as outcomes appear to

be analysed as SMD and converted to Cohen's d, rather than as binary outcomes which one would presume a suicide attempt or completion is.

R: We would like to thank the reviewer for pinpointing this aspect. We provided further information on the outcomes in the Methods section. Family records were considered as non-eligible. We chose to convert the outcomes to Cohen's d to be able to perform a meta regression, which would not be possible if we analysed Odds Ratio's. Moreover, by analysing Cohens d we will be able to compare our study with other mental health care review studies, which mostly report effect sizes in Cohens d as well.

We added the following in the Methods section:

- *Page 7, paragraph Data items: Outcomes were completed or attempted suicides in quantitative measures, as defined by healthcare professionals (hospital records, questionnaires, or interview) or coroners records, as can be seen in Table 1 and 2.*

For the effect sizes that are only mentioned in text and not provided as a CMA figure, it would be easier to follow if some information as provided in a table or combined forest plot (done with excel), showing the n studies and heterogeneity statistics as well as effect sizes.

R: We thank the reviewer for this suggestion. We created new forest plots in excel, and provided relevant information.

Minor points

Possibly either the aim or objectives could be omitted at the end of the intro to avoid repetition.

R: We agree with the reviewer that the aim and objectives created repetition. Therefore, we moved the aim from the Introduction to the start of the Discussion, and changed the sentence to past tense.

We added the following to the Discussion:

- *Page 24: The aim of this review was to evaluate the effectiveness of suicide prevention interventions in different settings, to compare their relative effectiveness by providing an estimate of their effect size, and to explore possible synergism of multilevel interventions in a meta-analysis.*

Presumably peer reviewers are blinded to the PROSPERO ID?

R: As the review process of General Hospital Psychiatry is blinded, we were asked to submit a blinded manuscript (without author details). Identifying information is provided in the PROSPERO register, and hence we blinded the PROSPERO ID in our manuscript.

The reason for exclusion of Pearson et al. (2017) should be listed in the Flow chart.

R: We added a brief mention in the PRISMA figure of why the study of Person et al. 2017 was excluded.

We added the following in Figure 1:

- *Could not be pooled due to different outcomes (n = 1)*

Suggest using 'to' when reporting negative confidence intervals in text.

R: We thank the reviewer for this suggestion. For the clarity for the reader, however, we would like to maintain a uniform notation in reporting positive and negative confidence intervals. Hence, we would like to maintain the use of semicolons.

The conclusion "To conclude…." Is not the last para, please move accordingly.

R: We added a Conclusion paragraph in the Discussion, and we moved the conclusion of our study to this paragraph. Therefore, we removed 'To conclude' of the sentence.

We added a Conclusion paragraph in the Discussion

Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis

Article data: figures: 6; tables: 3; appendices: 2; word length article text: 4916; word length abstract: 224

Abstract

Objective: This study provides an estimate of the effect size of suicide prevention interventions and evaluates the possible synergistic effects of multilevel interventions. **Method:** A systematic review and meta-analysis were conducted of controlled studies evaluating suicide prevention interventions versus control published between 2011–2017 in PubMed, PsycINFO, and Cochrane databases. Data extraction and risk of bias assessment according to ROBINS criteria were performed by independent assessors. Cohen's delta was calculated by a random meta-analysis on completed and attempted suicides as outcomes. Meta-regression explored a possible synergistic effect in multilevel interventions. PROSPERO ID number: X. **Results:** The search yielded 16 controlled studies with a total of 252,932 participants. The meta-analysis was performed in 15 studies with 29,071 participants. A significant effect was found for suicide prevention interventions on completed suicides (*d*=-0.535, 95% CI -0.898; -0.171, *p*=.004) and on suicide attempts (*d*=-0.449, 95% CI -0.618; -0.280, *p*<.001). Regarding the synergistic effect of multilevel interventions, meta-regression showed a significantly higher effect related to the number of levels of the intervention (*p*=.032). **Conclusions:** Suicide prevention interventions are effective in preventing completed and attempted suicides and should be widely implemented. Further research should focus on multilevel interventions due to their greater effects and synergistic potential. ~~Multilevel interventions should be the strategy of choice due to a greater effect and a synergistic potential.~~ Further research is also needed into risk appraisal for completed versus attempted suicide, as the preferred intervention strategy differs with regard to both outcomes.

Keywords: suicide prevention, intervention, effectiveness, synergism, systematic review, meta-analysis, controlled studies

Introduction

RATIONALE

Suicide is a worldwide major public health problem, with 800,000 suicides annually.[1] Suicide attempts are among ~~,~~ the most important known predictors of completed suicides, and occur even more often.[1,2] Since the 2013 commitment of the World Health Organisation Member States to work towards suicide prevention,[3] ample national strategies and suicide prevention interventions have been developed and overviews of them provided in systematic reviews.[4-17] The effectiveness of suicide prevention interventions in reducing suicide rates is found in certain settings, but not (yet) in others.[4,8,11,12] In 2005, Mann et al. performed a systematic review pertaining to suicide prevention strategies in general;[18] this review was updated by Zalsman et al. in 2016.[4] Despite growing evidence for the effectiveness of several suicide prevention strategies, until now a comparative estimate for the effect of different types of interventions has not yet been provided. ~~Despite growing evidence for the effectiveness of several suicide prevention strategies, until now an estimate of the effect size has not been provided.~~ Also, it remains unclear which strategy is the most effective and if the setting of intervention is relevant to the effect.

It has been argued that effective action towards reducing suicide would need combined interventions by different providers in multiple domains[3,4,18] – so-called multilevel interventions.[19,20] For example, at the community level, this could be accomplished by: (1) providing gatekeepers such as teachers and with priests training others to aid recognition of persons potentially at risk; (2) combining it with a publicity campaign[21,22] and with (3) instructions to the press on how to publish information on suicides. In addition, on the primary care level, general practitioners could be trained on how to address ~~suicidality~~ suicidal thoughts and behaviour in patients. Indications of the effectivity of multilevel interventions were found in non-controlled studies;[20,23,24] however, this effect was not

replicated in one of the very few published randomised controlled trials examining the effectiveness of a multilevel intervention in preventing suicidal behaviour.[22]

Multilevel interventions have been suggested as having synergistic potential,[19] meaning that the effect of the combined parts of the intervention might create a stronger effect than the sum of the individual effects of the interventions. Hegerl et al. (2006) observed, during the implementation of a four-level community-based suicide prevention intervention, that general practitioners were more motivated to participate in the training sessions because the ongoing public campaign aimed at destigmatisation prompted their patients to present themselves with possible depressive symptoms and suicidal ideation.[24] Synergistic interactions between intervention levels were also suggested by a qualitative study on multilevel suicide prevention interventions in four European countries.[25] However, thus an estimate of a possible synergistic effect has not been provided.[19,20] ~~The aim of this review is to evaluate the effectiveness of suicide prevention interventions in different settings, to compare their relative effectiveness by providing an estimate of their effect size and to explore possible synergism of multilevel interventions in a meta-analysis.~~

OBJECTIVES

This study has three objectives:

1. To establish an estimate of the effect of suicide prevention interventions for completed suicides and suicide attempts;
2. To explore if the setting of intervention is associated with different effect sizes;
3. To explore if multilevel interventions have synergistic effects.

Methods

Protocol and registration

The study protocol is registered in PROSPERO, the international prospective register of systematic reviews of the University of York (www.crd.york.ac.uk/prospero/) and is accessible under ID number X. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for transparent reporting was followed.[26] The PRISMA checklist is included in Appendix 1.

Eligibility criteria

Studies were considered eligible if suicides and/or suicide attempts were included as an outcome and if a suicide prevention intervention was compared with a control group or period. ~~Eligible studies should report on suicides and/or on suicide attempts as an outcome. They should compare a suicide prevention intervention with a control group or period.~~ Studies were included when randomisation was performed between patients or between practice settings,[27] but could also be Controlled Cohort Studies (CCS), Controlled Before After studies (CBAs), Controlled Interrupted Time Series (CITS), or Interrupted Time Series (ITS) studies. Principal outcomes were suicide attempts and completed suicides and had to be defined in quantitative measures in order to make meta-analysis possible. The exclusion criterion was the inclusion of self-harm (non-suicidal self-injury; SH) in the target group for the intervention. ~~The exclusion criterion was the inclusion of self-harm (SH) in the target group for the intervention.~~

Information sources

Potentially eligible studies were identified by searching the databases PubMed, PsycINFO and the total database of the Cochrane Library (including Cochrane Database of Systematic

Reviews, Database of Abstracts of Reviews of Effect, Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, and NHS Economic Evaluation Database). As this study further elaborates on the systematic review of van der Feltz-Cornelis, which was published in 2011, our search extended from January 2011 through December 2017.[19] The reference lists of reviews were checked for missed studies. Personal files of the workgroup members were checked for relevant publications, and experts from the section suicidology and suicide prevention of the European Psychiatric Association (https://suicidologysection.org) and from the European Alliance Against Depression (EAAD) (www.eaad.net) were consulted about relevant publications in order to identify additional studies not found by our search strategy.

Search

A search was performed of systematic reviews of randomised or controlled studies in the field of suicide prevention interventions with MeSH terms and free text terms for 'suicide prevention' AND 'intervention' AND 'systematic review'. A second search was run with 'suicide prevention' AND 'intervention' AND 'clinical trial'. Randomised or controlled studies in the field of suicide prevention interventions were included. Only studies with a primary focus on suicide reduction were selected. The search strategy for PubMed is shown in Appendix 2. It was adapted for the other databases. We did not use language restrictions to minimise 'Tower of Babel Bias'.[28]

Study selection

After identifying studies from database searching and additional sources, duplicate records were removed. The titles and abstracts of the records were assessed to determine eligibility in a first screening and the full-text articles were assessed for eligibility in a second screening.

The screenings were performed in duplicate (X and X). If the two independent assessors had disagreements in coding, a third assessor (X) was consulted to make the final decision.

Data collection process

An overview of participants, interventions, comparisons, outcomes and study design (PICOS) is shown in Tables 1 and 2. The extraction of data was performed independently by two researchers (X and X). In the case of non-consensus, a third assessor (X) was consulted to make the final decision.

Data items

Two tables are provided, one for studies evaluating completed suicides and one for suicide attempts. Interventions are categorised as one level or multilevel, and the number of levels is provided by the third researcher of this study (X). The data items of each study are described below.

Type of study design

Included studies could be Randomised Controlled Trials, Cluster Randomised Controlled Trials, Controlled Cohort studies (CCs), Controlled Before After studies (CBAs), Controlled Interrupted Time Series (CITS) or Interrupted Time Series (ITS) studies.

Details of the intervention

Suicide prevention strategies may include community approaches, psychotherapeutic interventions, pharmacotherapeutic and multilevel interventions, with the prerequisite for inclusion that the intervention is sufficiently described to classify it as a suicide prevention intervention aimed at reducing attempted or completed suicides. The number of intervention

levels was taken into account in the analysis, as was the setting, which could be the community, emergency room, outpatient specialty mental health setting or a psychiatric ward in a general hospital.

Patient groups

Targeted populations could be suicidal persons in the various settings mentioned above; psychiatric patients, children and adolescents, older people, certain professional groups such as veterans, as well as ethnic minorities. There was no restriction on the kind of mental disorders.

Outcome definitions

Outcomes were completed or attempted suicides in quantitative measures, as defined by healthcare professionals (hospital records, questionnaires, or interview) or coroners records, as can be seen in Table 1 and 2. ~~Outcomes were completed or attempted suicides in quantitative measures.~~ Measurement instrument and follow-up time were recorded.

Level of evidence

Level of evidence was defined according to the criteria of the Oxford Centre of Evidence-Based Medicine.[29]

RISK OF BIAS IN INDIVIDUAL STUDIES

The quality of each study was determined by assessing the risk of bias in both the study and outcome level. Risk of bias (ROB) assessment was performed by two assessors (X, X) who discussed beforehand the required approach based upon the Cochrane Risk Of Bias in Non-randomised Studies – of Interventions (ROBINS-I)[30] and double-scored one of the articles. As

no particularities in assessment were observed, all the other studies were individually assessed by the two assessors. In ROB appraisal, as confounding factors, co-therapies such as pharmacotherapy or psychotherapy on top of the suicide prevention intervention were considered, as well as including both suicidal persons and persons performing self-harm in the study. In the case of RCTs, the most important Cochrane quality criterion, namely randomisation,[31,32] was explicitly mentioned. The results of this risk-of-bias assessment are shown in Table 3. Furthermore, a meta-regression explored if an association existed between the risk of bias of the studies and the effect size of the interventions.

Summary measures

We used the rates of completed or attempted suicides in intervention and control conditions for pooling. We calculated the effect sizes for each study using Comprehensive Meta-analysis version 2.[33] We chose to take the following outcome measures into account for the analysis:

1) As a first step, the combined effect on completed and attempted suicides was analysed and labeled suicidal behaviour.
2) Subsequently, separate analyses on those two outcomes were performed, with larger negative effect sizes being an improvement compared to smaller negative effect sizes, and effect sizes above zero a deterioration.

The effects were presented in terms of standardised effect sizes (Cohen's *d*). These effect sizes indicate by how many standard deviations the intervention group performed better than the control group. The effect size *d* is calculated by subtracting the average score of the control group (M_c) from the average score of the experimental group (M_e) and dividing the raw difference score by the pooled standard deviation of the experimental and control group.[34] An effect size of 0.5 indicates that the mean of the experimental group is half a standard deviation larger than the mean of the control group. In general, one considers an effect size of 0.56–1.2

a large clinical effect, an effect size of 0.33–0.55 moderate, and an effect size of 0–0.32 as small.[35,36]

Synthesis of results

We performed a random-effects meta-analysis to examine the effectiveness of interventions on suicide prevention.[37] Between-study heterogeneity was assessed using the Q-statistic,[38] which reflects the observed dispersion. In order to quantify this dispersion, the I^2 statistic was used, which describes the percentage of total variation across studies that is the result of heterogeneity rather than of chance. All statistical pooling was conducted using Comprehensive Meta-Analysis, version 2.[33]

Risk of bias across studies

Publication bias was examined by constructing a Begg funnel plot[39] and running a Stern & Egger test.[40]

Additional pre-envisioned moderator analyses

The setting of the intervention was explored as a moderator. Also, suicide prevention interventions were labelled as multilevel if they contained elements that were performed in different settings and by different providers.[19] Effect sizes of multilevel interventions were compared with effect sizes of non-multilevel interventions. In the case of multilevel interventions, an estimate of the effect was made to explore the potential of synergism by meta-regression. In the case of synergism, an exponential effect was expected.

Results

Study selection

The database search identified 442 records. In addition, 172 records were identified by consulting suicide prevention experts (19 records) and by identifying studies from literature reviews about suicide prevention interventions (153 records). After removal of duplicates, 447 records remained. After screening the records on title and abstract, 389 records were excluded and 58 articles were assessed for eligibility based on the full text (46 through database searching and 12 through additional sources). Finally, 16 studies were included in the systematic review. The study of Pearson et al. (2017) could not be pooled due to different outcomes, namely person-years. Hence, 15 studies were included in the meta-analysis, as is shown in Figure 1.

[Insert Figure 1 about here]

Figure 1. PRISMA flow diagram (2009) of the different phases of the systematic review

Study characteristics

An overview of the study and characteristics with regards to participants, interventions, comparisons, outcomes and study design (PICOS) for studies evaluating completed suicide and suicide attempts are presented in Tables 1 and 2. A total of 16 studies were included in the systematic review. Of these studies, 14 examined a unilevel suicide prevention intervention and two a multi-level intervention. Of the two multi-level interventions, one study included completed suicides as an outcome measure and one study attempted suicides.

Table 1. Overview of participants, interventions, comparisons, outcomes, and study design (PICOS) for studies evaluating completed suicide

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Unilevel		*N=234,589*				*d=-0.334 (95% CI -0.804; 0.136, p=.163)*
Vijayakumar et al., 2011[41]	RCT (1b)	- 622 participants in one general hospital (Admitted GHP) - India	Suicide attempters >12 years, admitted in a general hospital	Brief intervention and contact (BIC) (*n*=302) versus TAU (*n*=320)	- Study questionnaire - 18 months	Significant less suicides in BIC compared to control group (*d*= -1.193, CI -2.336; -0.051, *p*=.041).
Hvid et al., 2011[42 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 12 months	No significant difference between OPAC and control group (*d*=0.348, CI -0.989; 1.685, *p*=.610).
Wasserman et al., 2015[43]	Cluster-RCT (1b)	- 8,182 participants in 168 schools (Community level) - European Union (EU) countries	Adolescent pupils recruited from EU schools	Question, Persuade and Refer (*n*=1,978) and Youth Aware of Mental Health Programme (*n*=1,987) and screening by professionals (*n*=1,961) versus exposure to educational posters in the classroom (*n*=2,256)	- Paykel Hierarchical Suicidal Ladder[44] - 12 months	No significant difference between intervention groups and a control group (no participants completed suicide during the study period).[c]
Rudd et al., 2015[45]	RCT (1b)	- 108 participants in one Military Hospital (Outpatient SMHI) - USA	Active-duty Army soldiers with suicide attempt or ideation	Brief cognitive-behavioural therapy (BCBT) (*n*=54) versus TAU (*n*=54)	- Suicide Attempt Self-Injury Interview[46] - 24 months	No significant difference between BCBT and control group (*d*=0.000, CI -1.538; 1.538, *p*=1.000).
Amadéo et al., 2015[47]	RCT (1b)	- 190 participants in one hospital psychiatric emergency department (Admitted GHP) - French Polynesia	Patients who sought help due to non-fatal suicidal behaviour	Brief Intervention and Contact (BIC) (*n*=90) versus TAU (*n*=100)	- Coroner's records - 18 months	No significant difference between BIC and control group (*d*=-0.841, CI -2.522; 0.841, *p*=.327).
Lahoz et al., 2016[48 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI)	Suicide attempters arriving at the	Outreach, Problem solving, Adherence, Continuity	- Hospital records - 60 months	No significant difference between OPAC and control

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
		- Denmark	hospital ED and clinical departments	(OPAC) program (*n*=65) versus TAU (*n*=60)		group (*d*=-0.043, CI -1.140; 1.054, *p*=.939).
Miller et al., 2017[49]	PP (2c)	- 1,376 participants in 8 hospital ED's (ED) - USA	Adults with recent suicide attempt or ideation presented to hospital ED	Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) + Screening (*n*=502) or Screening alone (*n*=377) versus TAU (*n*=497)	- Columbia Suicide Severity Rating Scale[50] + medical records - 12 months	No significant difference between ED-SAFE and control group (*d*=-0.289, CI -1.082; 0.503, *p*=.474).
Pearson et al., 2017[51] [b]	Cluster-RCT (1b)	- 223,861 participants in the community (Community level) - Sri Lanka	People aged 14 years or older in households living in rural villages	Distribution and promotion of household lockable pesticide storage (*n*=114,168) versus usual practice (*n*=109,693)	- Hospital, community and coroner data - 36 months	No significant difference between the intervention group and the control group.[c]
Multilevel						
Three-level		*N=14,309*				*d=-0.832 (95% CI -1.406; -0.259, p=.004)*
Mishara et al., 2012[52]	PP (2c)	- 14,309 participants of all Montreal police and rest of Quebec police (QP) (Community level) - Canada	Montreal police (MP) officers	Together for Life in Montreal police (*n*=4,178) versus no intervention in rest of Quebec police (*n*=10,131)	- Quebec Coroner's Office on all police suicides - 144 months	Significant fewer suicides in intervention compared to control group (*d*=-0.832, CI -1.406; -0.259, *p*=.004).

Note: [a] The study of Lahoz et al., 2016 is a 5-year followup of the study of Hvid et al., 2011.

[b] The study of Pearson et al., 2017 reported in person-years and was not included in the meta-analysis.

[c] The study of Wasserman et al., 2015 and Pearson et al., 2017 were not included in the meta-analysis to completed suicides; effect size is therefore not provided in the table.

Abbreviations: ED = emergency department. GHP = psychiatric ward in general hospital. OPAC = suicide prevention intervention named Outreach, Problem-solving, Adherence, Continuity programme. PS = suicide prevention intervention named Screening by professionals. PP = pre-post design. QPR = suicide prevention intervention named Question, persuade and refer. RCT = randomised controlled trial. SMHI = specialty mental health institution. TAU = treatment as usual. YAM = suicide prevention intervention named Youth aware of mental health programme.

Table 2. Overview of participants, interventions, comparisons, outcomes, and study design (PICOS) for studies evaluating attempted suicide

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Unilevel		*N=237,387*				*d=-0.443 (95% CI -0.632 ;0.254, p<.001)*
Hassanian-Moghaddam et al., 2011[53]	RCT (1b)	- 2,113 participants in one poison Hospital ED (ED) - Iran	Suicide attempters by self-poisoning >12 years	Postcard intervention (*n*=1,043) versus TAU (*n*=1,070)	- Study questionnaire + hospital records - 12 months	Significant less suicide attempts in intervention compared to control group (*d*=-0.306, CI -0.544; -0.069, *p*=.012).
Vijayakumar et al., 2011[41]	RCT (1b)	- 622 participants in one general hospital (Admitted GHP) - India	Suicide attempters >12 years, admitted in a general hospital	Brief intervention and contact (BIC) (*n*=302) versus TAU (*n*=320)	- Study questionnaire - 18 months	No significant difference between BIC and control group (*d*=-0.399, CI -0.871; 0.073, *p*=.097).
Hvid et al., 2011[42a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 12 months	Significant less suicide attempts in OPAC compared to control group (*d*=-0.784, CI -1.434; -0.133, *p*=.018).
Cebrià et al., 2013[54]	CCS (3b)	- 514 participants in two hospital emergency departments (ED) - Spain	Suicide attempters discharged from ED	Systematic one-year telephone follow-up (*n*=296) versus TAU (*n*=218)	- Medical records - 12 months	Significant less suicide attempts in intervention compared to control group (*d*=-0.587, CI -0.935; -0.239, *p*=.001).
Mousavi et al., 2014[55]	RCT (1b)	- 139 participants in one hospital ED (ED) - Iran	Suicide attempters >15 years, admitted to hospital ED	Brief interventional contact (BIC) (*n*=69) versus TAU (*n*=70)	- Study questionnaire - 6 months	No significant difference between BIC and control group (*d*=-0.781, CI -2.003; 0.442, *p*=.211).
Wasserman et al., 2015[43]	Cluster-RCT (1b)	- 8,182 participants in 168 schools (Community level) - European Union (EU) countries	Adolescent pupils recruited from EU schools	Question, Persuade and Refer (*n*=1,978) and Youth Aware of Mental Health Program (*n*=1,987) and screening by professionals (*n*=1,961) versus exposure to educational posters in the class room (*n*=2,256)	- Paykel Hierarchical Suicidal Ladder[44] - 12 months	Significant less suicide attempts in YAM compared to control group (*d*=-0.424, CI -0.768; -0.079, *p*=.016). No significant difference between PS and control group (*d*=-0.218, CI -0.524; 0.088, *p*=.163). No significant difference between QPR and control group (*d*=

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
						-0.170, CI -0.467; 0.128, *p*=.264).
Rudd et al., 2015[45]	RCT (1b)	- 108 participants in one military Hospital (Outpatient SMHI) - USA	Active-duty Army soldiers with suicide attempt or ideation	Brief cognitive-behavioural therapy (BCBT) (*n*=54) versus TAU (*n*=54)	- Suicide Attempt Self-Injury Interview[46] - 24 months	Significant less suicide attempts in BCBT compared to control group (*d*=-0.535, CI -1.033; -0.037, *p*=.035).
Gysin-Maillart et al., 2016[56]	RCT (1b)	- 103 participants in one psychiatric department General Hospital (Outpatient SMHI) - Switzerland	Suicide attempters admitted to ED	Attempted Suicide Short Intervention Programme (ASSIP) (*n*=56) versus TAU (*n*=47)	- Questionnaire - 24 months	Significant less suicide attempts in ASSIP compared to control group (*d*=-1.746, CI -2.333; -1.159, *p*<.001).
Lahoz et al., 2016[48 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 60 months	No significant difference between OPAC and control group (*d*=-0.146, CI -0.585; 0.294, *p*=.516).
Goodman et al., 2016[57]	RCT (1b)	- 47 participants in one veterans' outpatient medical center (Outpatient SMHI) - USA	High risk suicidal veterans, aged 18-55 years	Dialectical Behavioral Therapy (DBT) (*n*=27) versus TAU (*n*=20)	- Columbia–Suicide Severity Rating Scale[50] - 12 months	No significant difference between DBT and control group (*d*=-0.322, CI -1.146; 0.503, *p*=.444).
Bryan et al., 2017[58]	RCT (1b)	- 72 participants in one military medical clinic (Admitted GHP) - USA	Active duty U.S. Army Soldiers, aged 18+ with suicidal ideation or attempt	Crisis Response Planning standard (CRP-s) (*n*=23) and Crisis Response Planning enhanced (CRP-e) (*n*=24) versus Contract for Safety (CfS) (*n*=25)	- Suicide Attempt Self-Injury Interview[46] - 6 months	No significant difference between CRP and control group (*d*=-0.740, CI -1.567; 0.088, *p*=.080).
Miller et al., 2017[49]	PP (2c)	- 1,376 participants in 8 hospital ED's (ED) - USA	Adults with recent suicide attempt or ideation presented to hospital ED	Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) + Screening (*n*=502) or Screening alone (*n*=377) versus TAU (*n*=497)	- Columbia Suicide Severity Rating Scale[50] + medical records - 12 months	No significant difference between ED-SAFE and control group (*d*=-0.156, CI -0.326; 0.014, *p*=.072).

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Pearson et al., 2017[51 b]	Cluster-RCT (1b)	- 223,861 participants in the community (Community level) - Sri Lanka	People aged 14 years or older in households living in rural villages	Distribution and promotion of household lockable pesticide storage (*n*=114,168) versus usual practice (*n*=109,693)	- Hospital, community and coroner data - 36 months	No significant difference between the intervention group and the control group.[c]
Multilevel						
Two-level		*N=1,046*				*d=-0.622 (95% CI -1.034; -0.210, p=.003)*
Schilling et al., 2016[59]	Cluster-RCT (1b)	- 1,046 participants in 16 technical high school (Community level) - USA	Ninth grade students in technical high school	Signs of Suicide (SOS) (*n*=650) versus wait list control group (*n*=396)	- Single-item measure from the Youth Risk Behavior Survey[60] - 3 months	Significant less suicide attempts in SOS compared to control group (*d*=-0.622, CI -1.034; -0.210, *p*<.003).

Note: [a] The study of Lahoz et al., 2016 is a 5-year follow-up of the study of Hvid et al., 2011.

[b] The study of Pearson et al., 2017 reported in person-years and was not included in the meta-analysis.

[c] The study of Pearson et al., 2017 was not included in the meta-analysis to suicide attempts; effect size is therefore not provided in the table.

Abbreviations: CCS = case-control study. ED = emergency department. GHP = psychiatric ward in general hospital. OPAC = suicide prevention intervention named Outreach, Problem solving, Adherence, Continuity programme. PS = suicide prevention intervention named Screening by professionals. PP = pre-post design. QPR = suicide prevention intervention named Question, persuade and refer. RCT = randomised controlled trial. SMHI = specialty mental health institution. TAU = treatment as usual. YAM = suicide prevention intervention named Youth aware of mental health programme.

RISK OF BIAS WITHIN STUDIES

The quality ratings of the studies are shown in Table 3. Thirteen studies were randomised studies (RCTs). Two out of 16 studies (12.50%) had a low overall risk of bias, meaning that these studies 'were comparable to a well-performed randomised trial'.[61] Nine studies had a moderate overall risk of bias (56.25%), meaning that these studies 'provided sound evidence for a non-randomised study but cannot be considered comparable to a well-performed randomized trial'.[61] Five studies (31.25%) had a serious overall risk of bias, meaning that these studies 'had some important problems'.[61] No studies showed a critical risk of bias. All studies were considered of sound quality according to the guidelines of the Oxford Centre of Evidence-Based Medicine.[29] Hence, all studies were used in the analyses.

Table 3. Risk of bias within studies

Study	Random-isation	Confound-ing	Selection of participants	Classifi-cation of intervention	Deviation intended intervention	Missing data	Measure-ment of outcomes	Selection reported result	**Overall bias**	Comments
Amadéo et al., 2015[47]	Yes	Low	Low	Low	Low	Moderate	Low	Low	**Moderate**	Two-tailed test in spite of the apparently expected direction of the effect; small sample size; missing data.
Bryan et al., 2017[58]	Yes	Low	Moderate	Low	Moderate	Low	Low	Low	**Moderate**	Small sample size (*N*=97) and delay in interventions due to recruitment suspension (recruitment goal was *N*=360).
Cebrià et al., 2013[54]	No	Serious	Low	Low	Low	Low	Moderate	Low	**Serious**	No information about SH; outcome measure could have been influenced by knowledge of the intervention received in the experimental setting (change in 2008).
Goodman et al., 2016[57]	Yes	Moderate	Low	Low	Low	Serious	Low	Low	**Serious**	A high number of drop-out, no ITT/NTT; no information about SH.
Gysin-Maillart et al., 2016[56]	Yes	Low	Low	Low	Low	Moderate	Low	Low	**Moderate**	Missing data due to drop-out.
Hassanian-Moghaddam et al., 2011[53]	Yes	Low	Low	Low	Low	Low	Low	Low	**Low**	Good quality study.
Hvid et al., 2011[42]	Yes	Low	Low	Moderate	Low	Low	Moderate	Low	**Moderate**	Single-blind study; one catchment area so people might, by chance, know each other or meet in the hospital.
Lahoz et al., 2016[48]	Yes	Low	Low	Low	Low	Low	Low	Low	**Low**	Completed and attempted suicide was taken together as an outcome.
Miller et al., 2017[49]	No	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**	Time might have influenced outcomes, time and site (probably) not in final analysis, no information about validity and reliability measures; possible selection of analysis/covariates.
Mishara et al., 2012[52]	No	Moderate	Serious	Moderate	Low	Moderate	Low	Low	**Serious**	Various interventions in different fields, therefore no clearly defined intervention; no outcome data at follow-up; missing data.
Mousavi et al., 2014[55]	Yes	Low	Low	Moderate	Low	Low	Moderate	Low	**Moderate**	Randomisation after the first interview; randomisation, missing data and assessment of information are not clearly described.

Pearson et al., 2017[51]	Yes	Moderate	Low	Low	Low	Low	Low	Low	**Moderate**	Cluster RCT, although corrected in analyses.
Rudd et al., 2015[45]	Yes	Low	Low	Low	Low	Low	Low	Moderate	**Moderate**	Multiple analyses of the intervention-outcome relationship not registered; no significant effect on Fisher exact (two-tailed); analysis selection is possible.
Schilling et al., 2016[59]	Yes	Moderate	Low	Low	Low	Serious	Moderate	Low	**Serious**	Cluster RCT; only significant demographics were included; proportions of participants not given, but probably contrary; more missing items at pre-test; self-assessment.
Vijayakumar et al., 2011[41]	Yes	Low	Low	Low	Low	Moderate	Moderate	Low	**Moderate**	Some 5-10% lost to follow-up; more missing items in TAU-group which decreases the effect; potential bias in the measurement of outcomes.
Wasserman et al., 2015[43]	Yes	Low	Low	Low	Low	Moderate	Moderate	Low	**Moderate**	Cluster RCT; missing data; self-assessment.

Note: Confounding = pre-intervention bias due to confounding. Selection of participants = pre-intervention bias in the selection of participants into the study. Classification of intervention = at-intervention bias in classification of interventions. Deviation intended intervention = post-intervention bias due to deviations from intended interventions. Missing data = Post-intervention bias due to missing data. Measurement of outcomes = Post-intervention bias in measurement of outcomes. Selection reported result = Post-intervention bias in the selection of the reported result.[61]

Results of individual studies

A total of 16 studies with 252,932 participants were selected for the systematic review. All studies were published in the time period of 2011–2017. Thirteen studies were (cluster) randomised controlled trials (81.3%),[41-43,45,47,48,51,53,55-59] two studies were a pre-post design study (12.5%),[49,52] and one study was a case-controlled design (6.3%).[54] Fourteen interventions evaluated unilevel interventions (87.5%),[41-43,45,47-49,51,53-58] and two evaluated multilevel interventions (two-level: *n*=1, 6.3%[59]; three-level: *n*=1, 6.3%[52]). Two studies reported on the effect of suicide prevention interventions on completed suicides (12.5%),[47,52] seven studies on attempted suicides (43.8%)[53-59] and seven studies reported on both (43.8%).[41-43,45,48,49,51] In five of the 16 studies, the setting was an outpatient specialty mental health institution (31.3%),[42,45,48,56,57] in four studies an emergency department (25.0%)[49,53-55] or a community facility (25.0%) was involved,[43,51,52,59] and in three studies the setting was a psychiatric ward of a general hospital (18.8%).[41,47,58] Nine of 16 studies (56.3%) reported on participants who received treatment in a hospital (emergency room or psychiatric department) after non-fatal suicidal behaviour.[41,42,47-49,53-56] In four studies (25.0%) professional groups, such as soldiers, veterans and police officers, were involved.[45,52,57,58] Participants from the community, such as from schools, were reported in three studies (18.8%).[43,51,59]

Synthesis of results

Overall meta-analysis

The study of Pearson et al., 2017 reported in person-years and this outcome could not be pooled with the outcomes of the other studies. Hence that study was not included in the meta-analysis. A total of 15 studies were included in the meta-analysis, all together reporting 62 suicides and 1006 suicide attempts (participants might have attempted suicide multiple times).

The first meta-analysis established the overall effect of any kind of suicide prevention intervention on combined completed and attempted suicides, here defined as suicidal behaviour. Overall meta-analytic regression for this combined effect showed a significant, albeit moderate effect, with all studies favouring suicide prevention interventions over control conditions. The pooled estimate of effect size was d=-0.495 (95% CI -0.677; -0.313, p<.001). The forest plot is shown in Figure 2.

[Insert Figure 2 as online data supplement]

Figure 2. Forest plot suicidal behaviour

Heterogeneity (Q value) of this combined effect of suicide prevention interventions for all studies taken together was 32 (*df*=16, *p*=.011). The I^2 statistic was 50%, indicating moderate heterogeneity, sufficiently to use a random model to fit the data, which was done in this analysis (Higgins). Because of this Q value and I^2 level of heterogeneity of the combined outcomes, the further analyses were performed separately for completed suicides and attempted suicides.

Completed suicides

For suicide prevention interventions on completed suicides, the pooled estimate was *d*=-0.535 (95% CI -0.898; -0.171, *p*=.004), which is a large, statistically significant effect. This effect is larger than the abovementioned combined effect. Q value for these studies was 6 (*df*=6, *p*=.455). The I^2 statistic was 0%, indicating no heterogeneity. This is a robust effect. The forest plot is shown below.

[Insert Figure 3 about here]

Figure 3. Forest plot of completed suicides

Attempted suicides

For suicide prevention interventions on attempted suicides, the pooled estimate was d=-0.449 (95% CI -0.618; -0.280, p<.001), which is a moderate, statistically significant effect, slightly smaller than the above-mentioned combined effect. The forest plot is shown below. The Q value for these studies was 37 (df=14, p=.001). The I^2 statistic was 62%, indicating large heterogeneity.

[Insert Figure 4 about here]

Figure 4. Forest plot of attempted suicides

ADDITIONAL ANALYSIS

Setting of intervention

In order to establish whether outcomes differ across settings in which suicide prevention intervention is provided, a separate pre-envisioned moderator analysis of studies according to the type of setting was done. Results are shown separately for completed suicides and attempted suicides.

Completed suicides

For completed suicides, suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital show the highest effect: *d*=-1.082 (95% CI -2.027; -0.137, *p*=.025). This is a large effect. Next effective were community-level interventions, with *d*=-0.832 (95% CI -1.406; -0.259, *p*=.004), a large effect size. Emergency room setting suicide prevention interventions had a small, non-significant effect size of *d*=-0.289 (95% CI -1.082; 0.503, *p*=.474). Outpatient specialty mental health setting interventions had a worse outcome for suicide prevention interventions than the control, with an effect size of *d*=0.088 (95% CI -0.655; 0.831, *p*=.817); this effect was not significant. With the use of a random effects model, Q between groups was 5 (*df*=3, *p*=.145).

Attempted suicides

For attempted suicides, outpatient specialty mental health setting interventions showed the highest effect: *d*=-0.705 (95% CI -1.275; -0.135, *p*=.015). This is a large effect. Next best were suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital, with *d*=-0.483 (95% CI -0.892; -0.073, *p*=.021), a moderate effect size. Community-level interventions had an effect size of *d*=-0.324 (95% CI 0.513; -0.136, *p*=.001) and emergency room setting suicide prevention interventions had an effect size of *d*=-0.319 (95% CI -0.528; -0.110, *p*=.003). Both were small effects. With the use of a random effects model, Q between groups was 2 (*df*=3, *p*=.565).

Multilevel suicide prevention interventions

Suicide interventions were labelled as multilevel if they contained elements that were performed in different healthcare settings or domains and by different providers. Effect sizes in terms of completed suicides differed for multilevel interventions from non-multilevel interventions as follows: non-multilevel intervention effects were: *d*=-0.334 (95% CI -

0.804;0.136, *p*=.163) which was a small and non-significant effect. Multilevel interventions were: *d*=-0.832 (95% CI -1.406; -0.259, *p*=.004), which is a large, significant effect. Q between groups was 2 (*df*=1, *p*=.188). Effect sizes in terms of attempted suicides differed for multilevel interventions from non-multilevel interventions as follows: non-multilevel interventions: *d*=-0.443 (95% CI -0.632; -0.254, *p*<.001), which was a moderate and significant effect. Multilevel interventions were: *d*=-0.622 (95% CI -1.034; -0.210, *p*=.003) which was a large, significant effect. Q between groups was 0.598 (*df*=1, *p*=.438).

Synergistic effect

The meta-regression analysis examined whether a synergistic effect for multilevel suicide prevention interventions could be found on combined outcomes. The analysis showed a significant effect of the number of levels in the suicide prevention intervention on effect size (*Q*=4.591, *df*=1 *p*=.032). With single-level interventions, the effect size was -0.3, which is a small effect. Two-level interventions show an effect size of approximately -0.5, which is moderate, and three levels show a large effect, going up to -0.8, as can be seen in Figure 5.

[Insert Figure 5 about here]

Figure 5. Meta-regression of number of intervention levels on the standardised mean difference

RISK OF BIAS

Risk of bias within studies: meta-regression

As indicated on the Risk of Bias (ROB; Table 3), ROB varied greatly; moreover, there were a substantial number of studies with serious ROB. Hence, a meta-regression was performed to explore whether the level of ROB in the studies was associated with the effect as found in the analysis. The analysis showed that there was no significant association (Q =0.033, df=1 p=.855). Hence, all studies could be used for the analysis, as was done in this study.

Risk of bias across studies: publication bias

A test for publication bias was performed. The Begg funnel plot with observed and imputed studies is shown in Figure 6. It shows that the adjusted estimate is fairly close to the original. The Egger test was not significant, indicating symmetry (t(17)=1.620, 95% CI: -2.21; 0.29, p=.124). This indicates that no significant publication bias seems to be the case, and the reported effect is valid.

[Insert Figure 6 as Online data supplement]

Figure 6. Funnel plot

Discussion

The aim of this review was to evaluate the effectiveness of suicide prevention interventions in different settings, to compare their relative effectiveness by providing an estimate of their effect size, and to explore possible synergism of multilevel interventions in a meta-analysis. This systematic review includes 252,932 participants in 16 controlled studies. The meta-analysis, for the first time, provides a comparative estimate for the effect of different types of suicide prevention interventions, based on 15 controlled studies, with 29,071 participants in various settings. ~~The meta-analysis, for the first time, provides an estimate of the effect size of~~

~~suicide prevention interventions based on 15 controlled studies, with 29,071 participants in various settings.~~ The findings show that suicide prevention interventions are effective in preventing both completed and attempted suicides. The effect size for completed suicides is larger than for attempted suicides. It might seem counterintuitive that interventions effective against completed suicides do not always prevent suicide attempts, as the greatest risk of completed suicide are suicide attempts. However, a possible explanation might be that the profile of the patient group that attempts suicide may differ in terms of personality disorder or method of suicide. Therefore, it might be that a suicide prevention intervention that is effective against one is not automatically as effective against the other outcome. This may be related to findings that people who complete suicide, in comparison to people who attempt suicide, are more often middle- or elderly-aged men,[62,63] and choose lethal means – such as hanging – more frequently as the suicide method[62] ~~and have fewer psychiatric problems~~. People who attempt suicide are more often younger women,[62] and use less lethal means – such as overdose or cutting – as suicide method ~~and have more psychiatric problems~~.[62] More research is needed to whether individuals that complete versus attempt suicide differ with regards to the presence of psychiatric disorders.

Differences between completed suicides and attempted suicides can also be identified in terms of intervention settings. For completed suicides, suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital and community-level interventions showed large effects. Interventions in other settings showed no significant effect. However, in attempted suicides, suicide prevention interventions delivered in outpatient specialty mental health settings showed a large effect and, for patients admitted to a psychiatric ward in a general hospital, a moderate effect. Community level and emergency room-based interventions had only small effects. It is remarkable that, although an intervention provided in an outpatient specialty mental health institution might be very

effective in preventing suicide attempts, it might not at all be effective in preventing completed suicides. A very tentative explanation is that there are different patient profiles: a) patients who require an admission to advert suicide, and b) patients whose ~~suicidality~~ suicidal thoughts and behaviour might be related to a personality disorder or coping problems and who might benefit more from outpatient treatment. In the latter group, patients might be more amenable to interventions that foster individual autonomy. This finding is of high clinical and policy relevance as, until now, the general assumption in research has been that the interventions will work equally for both outcomes. It underscores the need to be able to discern risk for completed suicide from risk for attempted suicide in clinical practice. However, making such determinations remains a substantial clinical challenge.

The findings also show that multilevel interventions are more effective than single level interventions and, further, that effect size rises significantly with the number of levels involved. Regarding synergism, a synergistic effect of multilevel interventions would ideally occur when the combined effect of the interventions is greater than the sum of the individual effects. This could be expressed as an exponential relationship between the numbers of intervention levels. In this study, a more linear relationship was found. However, as the effect sizes were considerable, ranging from -0.3 to -0.5 and -0.8 for the three-level intervention, a ceiling effect might have occurred. Although this does not yet provide direct evidence for synergism as described above, the findings are promising. In view of the low number of studies with more than one level, further research into multilevel interventions is recommended. Due to the added value of multilevel interventions and the synergistic potential, we recommend the implementation of multilevel suicide prevention interventions above one level.

STRENGTHS AND LIMITATIONS

This study is the first to perform a systematic review and meta-analysis evaluating controlled studies examining the effect of any kind of suicide prevention intervention and providing an estimate of the effect size. The number of participants was high, 252,932, and the focus on quantitative outcomes for completed and attempted suicides enabled us to establish clear outcomes of high societal relevance. Moreover, despite completed suicides being a very low base rate behavior, we found significant results which is probably due to the very large number of patients that were included in our study. There were no indications for publication bias, and it is not expected that relevant studies were excluded or missed in the review process since the authors consulted multiple sources for the identification of studies. With regard to limitations, we compared the three intervention conditions that were examined in the Wasserman et al. (2015) study[43] separately, with the one control condition of their study for the meta-analysis, rather than comparing the three interventions together with the control condition. This was done to prevent the loss of relevant information, as there were differences in the interventions themselves and, importantly, also in their effectiveness in the prevention of suicide. A second limitation is that we only included two multilevel interventions in the meta-analysis of which one was a two-level intervention and one was a three-level intervention. Multilevel interventions should, therefore, be the focus of further research, as the current evidence indicates a greater effect of multilevel interventions compared to unilevel interventions and synergistic potential. Moreover, completed suicides remain a low base rate behavior. This resulted in our study in a less precise estimate of the effect, compared to suicide attempts. It is desirable for future research that more studies will examine the effect of suicide prevention interventions on preventing completed suicide, as more studies will enable more precise estimates of the effects.

FUTURE RESEARCH

Although the number of participants in this review was high (*N*=252,932), and the number included in the meta-analysis as well (N=29,071), the number of controlled studies reporting on completed or attempted suicides identified in this study (*N*=16) was lower than expected in view of the globally rising suicide rates and the 2013 commitment of the World Health Organisation Member States for the development of suicide prevention interventions. Many studies are non-controlled investigations that report on indirect precursors of suicide such as suicidal ideation. This might be due to the fact that suicide is a statistically rare event; however, preventing suicide should be the ultimate goal of a suicide prevention intervention. We, therefore, recommend future research with controlled designs to further examine the effectiveness of suicide prevention interventions – especially multilevel interventions – on numbers of completed or attempted suicides. Future research should also examine further differential effects across outcomes and across specific characteristics of settings. For example, for some people, a psychiatric admission might be very effective in preventing suicidal behaviours, while for others it might cause pervasive distress.[64] Also, some settings may have more effect on prevention of completed suicides, while others may be more effective for attempted suicides. More insight is needed into which characteristics contribute to making an intervention in a particular setting more or less effective, and in which respect. This study shows that the assumption that interventions have the same effect on completed and attempted suicides, and in different settings, is no longer valid. A related recommendation for future research would be to determine optimal strategies for professionals to discern risk for completed suicide from risk for an attempt, as appropriate interventions for each may differ. Finally, further research is needed to explore and further improve synergism in multilevel interventions.

Conclusion

~~To conclude, s~~Suicide prevention interventions are effective in preventing suicidal behavior and should be widely implemented. The findings suggest that clinicians should make an assessment of whether their patient is at serious risk for completing suicide. This will assist in determining the most appropriate treatment: intervention provided in the psychiatric ward of a general hospital or, alternatively, prevention of attempted suicide in an outpatient specialty mental health clinic. Moreover, multilevel interventions should be the focus of further research due to a greater effect and synergistic potential. ~~multilevel interventions should be the strategy of choice due to a greater effect and a synergistic potential.~~

Contributors

X and X designed the study. X, X and X performed the systematic review and data extraction. X and X assessed the risk of bias of individual studies. X performed the meta-analysis. X and X wrote the first draft of the paper, and X, X, X, X, and X contributed in the process of drafting and revising. All authors gave their agreement and approval for all aspects of the final version of the paper.

Declaration of interests and funding

The authors declare no competing interests. The authors of this study had full access to all the data in the study and had final responsibility for the integrity of the data, the accuracy of data analysis and the decision to submit for publication. This research was funded by the Netherlands Organisation for Health Research and Development, grant number X. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Appendix 1: PRISMA Checklist

Section/topic	#	Checklist item	Page
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	0
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2)	9

		for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	19
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	19
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	23
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	24
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policymakers).	24
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	27
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	29
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	29

Appendix 2: Search strategy

PubMed

#1 Systematic reviews

(‘suicide’[MeSH Terms] OR ‘suicide’[All Fields]) AND (‘prevention and control’[Subheading] OR (‘prevention’[All Fields] AND ‘control’[All Fields]) OR ‘prevention and control’[All Fields] OR ‘prevention’[All Fields]) AND (‘methods’[MeSH Terms] OR ‘methods’[All Fields] OR ‘intervention’[All Fields]) AND (‘review’[Publication Type] OR ‘review literature as topic’[MeSH Terms] OR ‘systematic review’[All Fields]) AND (‘2011/01/01’[PDAT] : ‘2017/12/15’[PDAT])

#2 Clinical trials

(‘suicide’[MeSH Terms] OR ‘suicide’[All Fields]) AND (‘prevention and control’[Subheading] OR (‘prevention’[All Fields] AND ‘control’[All Fields]) OR ‘prevention and control’[All Fields] OR ‘prevention’[All Fields]) AND (‘methods’[MeSH Terms] OR ‘methods’[All Fields] OR ‘intervention’[All Fields]) AND (‘clinical trial’[Publication Type] OR ‘clinical trials as topic’[MeSH Terms] OR ‘clinical trial’[All Fields]) AND (‘2011/01/01’[PDAT] : ‘2017/12/15’[PDAT])

The PubMed search strategy for systematic reviews and clinical trials was also translated for the PsycINFO and Cochrane databases.

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Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis

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Contributors

EH and CFC designed the study. EH, DÖ and CFC performed the systematic review and data extraction. ChvN and MB assessed the risk of bias of individual studies. CFC performed the meta-analysis. EH and CFC wrote the first draft of the paper, and ChvN, MB, IE, SdJ, and DÖ contributed in the process of drafting and revising. All authors gave their agreement and approval for all aspects of the final version of the paper.

Declaration of interests and funding

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Effectiveness of Suicide Prevention Interventions: A Systematic Review and Meta-Analysis

Article data: figures: 6; tables: 3; appendices: 2; word length article text: 4916; word length abstract: 224

Abstract

Objective: This study provides an estimate of the effect size of suicide prevention interventions and evaluates the possible synergistic effects of multilevel interventions. **Method:** A systematic review and meta-analysis were conducted of controlled studies evaluating suicide prevention interventions versus control published between 2011–2017 in PubMed, PsycINFO, and Cochrane databases. Data extraction and risk of bias assessment according to ROBINS criteria were performed by independent assessors. Cohen's delta was calculated by a random meta-analysis on completed and attempted suicides as outcomes. Meta-regression explored a possible synergistic effect in multilevel interventions. PROSPERO ID number: X. **Results:** The search yielded 16 controlled studies with a total of 252,932 participants. The meta-analysis was performed in 15 studies with 29,071 participants. A significant effect was found for suicide prevention interventions on completed suicides (d=-0.535, 95% CI -0.898; -0.171, p=.004) and on suicide attempts (d=-0.449, 95% CI -0.618; -0.280, p<.001). Regarding the synergistic effect of multilevel interventions, meta-regression showed a significantly higher effect related to the number of levels of the intervention (p=.032). **Conclusions:** Suicide prevention interventions are effective in preventing completed and attempted suicides and should be widely implemented. Further research should focus on multilevel interventions due to their greater effects and synergistic potential. Further research is also needed into risk appraisal for completed versus attempted suicide, as the preferred intervention strategy differs with regard to both outcomes.

Keywords: suicide prevention, intervention, effectiveness, synergism, systematic review, meta-analysis, controlled studies

Introduction

RATIONALE

Suicide is a worldwide major public health problem, with 800,000 suicides annually.[1] Suicide attempts are among the most important known predictors of completed suicides, and occur even more often.[1,2] Since the 2013 commitment of the World Health Organisation Member States to work towards suicide prevention,[3] ample national strategies and suicide prevention interventions have been developed and overviews of them provided in systematic reviews.[4-17] The effectiveness of suicide prevention interventions in reducing suicide rates is found in certain settings, but not (yet) in others.[4,8,11,12] In 2005, Mann et al. performed a systematic review pertaining to suicide prevention strategies in general;[18] this review was updated by Zalsman et al. in 2016.[4] Despite growing evidence for the effectiveness of several suicide prevention strategies, until now a comparative estimate for the effect of different types of interventions has not yet been provided. Also, it remains unclear which strategy is the most effective and if the setting of intervention is relevant to the effect.

It has been argued that effective action towards reducing suicide would need combined interventions by different providers in multiple domains[3,4,18] – so-called multilevel interventions.[19,20] For example, at the community level, this could be accomplished by: (1) providing gatekeepers such as teachers and with priests training others to aid recognition of persons potentially at risk; (2) combining it with a publicity campaign[21,22] and with (3) instructions to the press on how to publish information on suicides. In addition, on the primary care level, general practitioners could be trained on how to address suicidal thoughts and behaviour in patients. Indications of the effectivity of multilevel interventions were found in non-controlled studies;[20,23,24] however, this effect was not replicated in one of the very few published randomised controlled trials examining the effectiveness of a multilevel intervention in preventing suicidal behaviour.[22]

Multilevel interventions have been suggested as having synergistic potential,[19] meaning that the effect of the combined parts of the intervention might create a stronger effect than the sum of the individual effects of the interventions. Hegerl et al. (2006) observed, during the implementation of a four-level community-based suicide prevention intervention, that general practitioners were more motivated to participate in the training sessions because the ongoing public campaign aimed at destigmatisation prompted their patients to present themselves with possible depressive symptoms and suicidal ideation.[24] Synergistic interactions between intervention levels were also suggested by a qualitative study on multilevel suicide prevention interventions in four European countries.[25] However, thus an estimate of a possible synergistic effect has not been provided.[19,20]

Objectives

This study has three objectives:

1. To establish an estimate of the effect of suicide prevention interventions for completed suicides and suicide attempts;
2. To explore if the setting of intervention is associated with different effect sizes;
3. To explore if multilevel interventions have synergistic effects.

Methods

Protocol and registration

The study protocol is registered in PROSPERO, the international prospective register of systematic reviews of the University of York (www.crd.york.ac.uk/prospero/) and is accessible under ID number X. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for transparent reporting was followed.[26] The PRISMA checklist is included in Appendix 1.

Eligibility criteria

Studies were considered eligible if suicides and/or suicide attempts were included as an outcome and if a suicide prevention intervention was compared with a control group or period. Studies were included when randomisation was performed between patients or between practice settings,[27] but could also be Controlled Cohort Studies (CCS), Controlled Before After studies (CBAs), Controlled Interrupted Time Series (CITS), or Interrupted Time Series (ITS) studies. Principal outcomes were suicide attempts and completed suicides and had to be defined in quantitative measures in order to make meta-analysis possible. The exclusion criterion was the inclusion of self-harm (non-suicidal self-injury; SH) in the target group for the intervention.

Information sources

Potentially eligible studies were identified by searching the databases PubMed, PsycINFO and the total database of the Cochrane Library (including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effect, Cochrane Central Register of Controlled Trials, Health Technology Assessment Database, and NHS Economic Evaluation Database). As this study further elaborates on the systematic review of van der Feltz-Cornelis, which was published in 2011, our search extended from January 2011 through December 2017.[19] The reference lists of reviews were checked for missed studies. Personal files of the workgroup members were checked for relevant publications, and experts from the section suicidology and suicide prevention of the European Psychiatric Association (https://suicidologysection.org) and from the European Alliance Against Depression (EAAD) (www.eaad.net) were consulted about relevant publications in order to identify additional studies not found by our search strategy.

Search

A search was performed of systematic reviews of randomised or controlled studies in the field of suicide prevention interventions with MeSH terms and free text terms for 'suicide prevention' AND 'intervention' AND 'systematic review'. A second search was run with 'suicide prevention' AND 'intervention' AND 'clinical trial'. Randomised or controlled studies in the field of suicide prevention interventions were included. Only studies with a primary focus on suicide reduction were selected. The search strategy for PubMed is shown in Appendix 2. It was adapted for the other databases. We did not use language restrictions to minimise 'Tower of Babel Bias'.[28]

Study selection

After identifying studies from database searching and additional sources, duplicate records were removed. The titles and abstracts of the records were assessed to determine eligibility in a first screening and the full-text articles were assessed for eligibility in a second screening. The screenings were performed in duplicate (X and X). If the two independent assessors had disagreements in coding, a third assessor (X) was consulted to make the final decision.

Data collection process

An overview of participants, interventions, comparisons, outcomes and study design (PICOS) is shown in Tables 1 and 2. The extraction of data was performed independently by two researchers (X and X). In the case of non-consensus, a third assessor (X) was consulted to make the final decision.

DATA ITEMS

Two tables are provided, one for studies evaluating completed suicides and one for suicide attempts. Interventions are categorised as one level or multilevel, and the number of levels is provided by the third researcher of this study (X). The data items of each study are described below.

Type of study design

Included studies could be Randomised Controlled Trials, Cluster Randomised Controlled Trials, Controlled Cohort studies (CCs), Controlled Before After studies (CBAs), Controlled Interrupted Time Series (CITS) or Interrupted Time Series (ITS) studies.

Details of the intervention

Suicide prevention strategies may include community approaches, psychotherapeutic interventions, pharmacotherapeutic and multilevel interventions, with the prerequisite for inclusion that the intervention is sufficiently described to classify it as a suicide prevention intervention aimed at reducing attempted or completed suicides. The number of intervention levels was taken into account in the analysis, as was the setting, which could be the community, emergency room, outpatient specialty mental health setting or a psychiatric ward in a general hospital.

Patient groups

Targeted populations could be suicidal persons in the various settings mentioned above; psychiatric patients, children and adolescents, older people, certain professional groups such as veterans, as well as ethnic minorities. There was no restriction on the kind of mental disorders.

Outcome definitions

Outcomes were completed or attempted suicides in quantitative measures, as defined by healthcare professionals (hospital records, questionnaires, or interview) or coroners records, as can be seen in Table 1 and 2. Measurement instrument and follow-up time were recorded.

Level of evidence

Level of evidence was defined according to the criteria of the Oxford Centre of Evidence-Based Medicine.[29]

RISK OF BIAS IN INDIVIDUAL STUDIES

The quality of each study was determined by assessing the risk of bias in both the study and outcome level. Risk of bias (ROB) assessment was performed by two assessors (X, X) who discussed beforehand the required approach based upon the Cochrane Risk Of Bias in Non-randomised Studies – of Interventions (ROBINS-I)[30] and double-scored one of the articles. As no particularities in assessment were observed, all the other studies were individually assessed by the two assessors. In ROB appraisal, as confounding factors, co-therapies such as pharmacotherapy or psychotherapy on top of the suicide prevention intervention were considered, as well as including both suicidal persons and persons performing self-harm in the study. In the case of RCTs, the most important Cochrane quality criterion, namely randomisation,[31,32] was explicitly mentioned. The results of this risk-of-bias assessment are shown in Table 3. Furthermore, a meta-regression explored if an association existed between the risk of bias of the studies and the effect size of the interventions.

SUMMARY MEASURES

We used the rates of completed or attempted suicides in intervention and control conditions for pooling. We calculated the effect sizes for each study using Comprehensive Meta-analysis version 2.[33] We chose to take the following outcome measures into account for the analysis:

1) As a first step, the combined effect on completed and attempted suicides was analysed and labeled suicidal behaviour.
2) Subsequently, separate analyses on those two outcomes were performed, with larger negative effect sizes being an improvement compared to smaller negative effect sizes, and effect sizes above zero a deterioration.

The effects were presented in terms of standardised effect sizes (Cohen's *d*). These effect sizes indicate by how many standard deviations the intervention group performed better than the control group. The effect size *d* is calculated by subtracting the average score of the control group (M_c) from the average score of the experimental group (M_e) and dividing the raw difference score by the pooled standard deviation of the experimental and control group.[34] An effect size of 0.5 indicates that the mean of the experimental group is half a standard deviation larger than the mean of the control group. In general, one considers an effect size of 0.56–1.2 a large clinical effect, an effect size of 0.33–0.55 moderate, and an effect size of 0–0.32 as small.[35,36]

SYNTHESIS OF RESULTS

We performed a random-effects meta-analysis to examine the effectiveness of interventions on suicide prevention.[37] Between-study heterogeneity was assessed using the Q-statistic,[38] which reflects the observed dispersion. In order to quantify this dispersion, the I^2 statistic was used, which describes the percentage of total variation across studies that is the result of

heterogeneity rather than of chance. All statistical pooling was conducted using Comprehensive Meta-Analysis, version 2.[33]

Risk of bias across studies

Publication bias was examined by constructing a Begg funnel plot[39] and running a Stern & Egger test.[40]

Additional pre-envisioned moderator analyses

The setting of the intervention was explored as a moderator. Also, suicide prevention interventions were labelled as multilevel if they contained elements that were performed in different settings and by different providers.[19] Effect sizes of multilevel interventions were compared with effect sizes of non-multilevel interventions. In the case of multilevel interventions, an estimate of the effect was made to explore the potential of synergism by meta-regression. In the case of synergism, an exponential effect was expected.

Results

Study selection

The database search identified 442 records. In addition, 172 records were identified by consulting suicide prevention experts (19 records) and by identifying studies from literature reviews about suicide prevention interventions (153 records). After removal of duplicates, 447 records remained. After screening the records on title and abstract, 389 records were excluded and 58 articles were assessed for eligibility based on the full text (46 through database searching and 12 through additional sources). Finally, 16 studies were included in the systematic review. The study of Pearson et al. (2017) could not be pooled due to different

outcomes, namely person-years. Hence, 15 studies were included in the meta-analysis, as is shown in Figure 1.

[Insert Figure 1 about here]

Figure 1. PRISMA flow diagram (2009) of the different phases of the systematic review

STUDY CHARACTERISTICS

An overview of the study and characteristics with regards to participants, interventions, comparisons, outcomes and study design (PICOS) for studies evaluating completed suicide and suicide attempts are presented in Tables 1 and 2. A total of 16 studies were included in the systematic review. Of these studies, 14 examined a unilevel suicide prevention intervention and two a multi-level intervention. Of the two multi-level interventions, one study included completed suicides as an outcome measure and one study attempted suicides.

Table 1. Overview of participants, interventions, comparisons, outcomes, and study design (PICOS) for studies evaluating completed suicide

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Unilevel		*N=234,589*				*d=-0.334 (95% CI -0.804; 0.136, p=.163)*
Vijayakumar et al., 2011[41]	RCT (1b)	- 622 participants in one general hospital (Admitted GHP) - India	Suicide attempters >12 years, admitted in a general hospital	Brief intervention and contact (BIC) (*n*=302) versus TAU (*n*=320)	- Study questionnaire - 18 months	Significant less suicides in BIC compared to control group (*d*= -1.193, CI -2.336; -0.051, *p*=.041).
Hvid et al., 2011[42 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 12 months	No significant difference between OPAC and control group (*d*=0.348, CI -0.989; 1.685, *p*=.610).
Wasserman et al., 2015[43]	Cluster-RCT (1b)	- 8,182 participants in 168 schools (Community level) - European Union (EU) countries	Adolescent pupils recruited from EU schools	Question, Persuade and Refer (*n*=1,978) and Youth Aware of Mental Health Programme (*n*=1,987) and screening by professionals (*n*=1,961) versus exposure to educational posters in the classroom (*n*=2,256)	- Paykel Hierarchical Suicidal Ladder[44] - 12 months	No significant difference between intervention groups and a control group (no participants completed suicide during the study period).[c]
Rudd et al., 2015[45]	RCT (1b)	- 108 participants in one Military Hospital (Outpatient SMHI) - USA	Active-duty Army soldiers with suicide attempt or ideation	Brief cognitive-behavioural therapy (BCBT) (*n*=54) versus TAU (*n*=54)	- Suicide Attempt Self-Injury Interview[46] - 24 months	No significant difference between BCBT and control group (*d*=0.000, CI -1.538; 1.538, *p*=1.000).
Amadéo et al., 2015[47]	RCT (1b)	- 190 participants in one hospital psychiatric emergency department (Admitted GHP) - French Polynesia	Patients who sought help due to non-fatal suicidal behaviour	Brief Intervention and Contact (BIC) (*n*=90) versus TAU (*n*=100)	- Coroner's records - 18 months	No significant difference between BIC and control group (*d*=-0.841, CI -2.522; 0.841, *p*=.327).
Lahoz et al., 2016[48 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI)	Suicide attempters arriving at the	Outreach, Problem solving, Adherence, Continuity	- Hospital records - 60 months	No significant difference between OPAC and control

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
		- Denmark	hospital ED and clinical departments	(OPAC) program (*n*=65) versus TAU (*n*=60)		group (*d*=-0.043, CI -1.140; 1.054, *p*=.939).
Miller et al., 2017[49]	PP (2c)	- 1,376 participants in 8 hospital ED's (ED) - USA	Adults with recent suicide attempt or ideation presented to hospital ED	Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) + Screening (*n*=502) or Screening alone (*n*=377) versus TAU (*n*=497)	- Columbia Suicide Severity Rating Scale[50] + medical records - 12 months	No significant difference between ED-SAFE and control group (*d*=-0.289, CI -1.082; 0.503, *p*=.474).
Pearson et al., 2017[51] [b]	Cluster-RCT (1b)	- 223,861 participants in the community (Community level) - Sri Lanka	People aged 14 years or older in households living in rural villages	Distribution and promotion of household lockable pesticide storage (*n*=114,168) versus usual practice (*n*=109,693)	- Hospital, community and coroner data - 36 months	No significant difference between the intervention group and the control group.[c]
Multilevel						
Three-level		*N=14,309*				*d=-0.832 (95% CI -1.406; -0.259, p=.004)*
Mishara et al., 2012[52]	PP (2c)	- 14,309 participants of all Montreal police and rest of Quebec police (QP) (Community level) - Canada	Montreal police (MP) officers	Together for Life in Montreal police (*n*=4,178) versus no intervention in rest of Quebec police (*n*=10,131)	- Quebec Coroner's Office on all police suicides - 144 months	Significant fewer suicides in intervention compared to control group (*d*=-0.832, CI -1.406; -0.259, *p*=.004).

Note: [a] The study of Lahoz et al., 2016 is a 5-year followup of the study of Hvid et al., 2011.

[b] The study of Pearson et al., 2017 reported in person-years and was not included in the meta-analysis.

[c] The study of Wasserman et al., 2015 and Pearson et al., 2017 were not included in the meta-analysis to completed suicides; effect size is therefore not provided in the table.

Abbreviations: ED = emergency department. GHP = psychiatric ward in general hospital. OPAC = suicide prevention intervention named Outreach, Problem-solving, Adherence, Continuity programme. PS = suicide prevention intervention named Screening by professionals. PP = pre-post design. QPR = suicide prevention intervention named Question, persuade and refer. RCT = randomised controlled trial. SMHI = specialty mental health institution. TAU = treatment as usual. YAM = suicide prevention intervention named Youth aware of mental health programme.

Table 2. Overview of participants, interventions, comparisons, outcomes, and study design (PICOS) for studies evaluating attempted suicide

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Unilevel		*N=237,387*				*d=-0.443 (95% CI -0.632 ;0.254, p<.001)*
Hassanian-Moghaddam et al., 2011[53]	RCT (1b)	- 2,113 participants in one poison Hospital ED (ED) - Iran	Suicide attempters by self-poisoning >12 years	Postcard intervention (*n*=1,043) versus TAU (*n*=1,070)	- Study questionnaire + hospital records - 12 months	Significant less suicide attempts in intervention compared to control group (*d*=-0.306, CI -0.544; -0.069, *p*=.012).
Vijayakumar et al., 2011[41]	RCT (1b)	- 622 participants in one general hospital (Admitted GHP) - India	Suicide attempters >12 years, admitted in a general hospital	Brief intervention and contact (BIC) (*n*=302) versus TAU (*n*=320)	- Study questionnaire - 18 months	No significant difference between BIC and control group (*d*=-0.399, CI -0.871; 0.073, *p*=.097).
Hvid et al., 2011[42a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 12 months	Significant less suicide attempts in OPAC compared to control group (*d*=-0.784, CI -1.434; -0.133, *p*=.018).
Cebrià et al., 2013[54]	CCS (3b)	- 514 participants in two hospital emergency departments (ED) - Spain	Suicide attempters discharged from ED	Systematic one-year telephone follow-up (*n*=296) versus TAU (*n*=218)	- Medical records - 12 months	Significant less suicide attempts in intervention compared to control group (*d*=-0.587, CI -0.935; -0.239, *p*=.001).
Mousavi et al., 2014[55]	RCT (1b)	- 139 participants in one hospital ED (ED) - Iran	Suicide attempters >15 years, admitted to hospital ED	Brief interventional contact (BIC) (*n*=69) versus TAU (*n*=70)	- Study questionnaire - 6 months	No significant difference between BIC and control group (*d*=-0.781, CI -2.003; 0.442, *p*=.211).
Wasserman et al., 2015[43]	Cluster-RCT (1b)	- 8,182 participants in 168 schools (Community level) - European Union (EU) countries	Adolescent pupils recruited from EU schools	Question, Persuade and Refer (*n*=1,978) and Youth Aware of Mental Health Program (*n*=1,987) and screening by professionals (*n*=1,961) versus exposure to educational posters in the class room (*n*=2,256)	- Paykel Hierarchical Suicidal Ladder[44] - 12 months	Significant less suicide attempts in YAM compared to control group (*d*=-0.424, CI -0.768; -0.079, *p*=.016). No significant difference between PS and control group (*d*=-0.218, CI -0.524; 0.088, *p*=.163). No significant difference between QPR and control group (*d*=

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
						-0.170, CI -0.467; 0.128, *p*=.264).
Rudd et al., 2015[45]	RCT (1b)	- 108 participants in one military Hospital (Outpatient SMHI) - USA	Active-duty Army soldiers with suicide attempt or ideation	Brief cognitive-behavioural therapy (BCBT) (*n*=54) versus TAU (*n*=54)	- Suicide Attempt Self-Injury Interview[46] - 24 months	Significant less suicide attempts in BCBT compared to control group (*d*=-0.535, CI -1.033; -0.037, *p*=.035).
Gysin-Maillart et al., 2016[56]	RCT (1b)	- 103 participants in one psychiatric department General Hospital (Outpatient SMHI) - Switzerland	Suicide attempters admitted to ED	Attempted Suicide Short Intervention Programme (ASSIP) (*n*=56) versus TAU (*n*=47)	- Questionnaire - 24 months	Significant less suicide attempts in ASSIP compared to control group (*d*=-1.746, CI -2.333; -1.159, *p*<.001).
Lahoz et al., 2016[48 a]	RCT (1b)	- 125 participants in one psychiatric outpatient setting (Outpatient SMHI) - Denmark	Suicide attempters arriving at the hospital ED and clinical departments	Outreach, Problem solving, Adherence, Continuity (OPAC) programme (*n*=65) versus TAU (*n*=60)	- Hospital records - 60 months	No significant difference between OPAC and control group (*d*=-0.146, CI -0.585; 0.294, *p*=.516).
Goodman et al., 2016[57]	RCT (1b)	- 47 participants in one veterans' outpatient medical center (Outpatient SMHI) - USA	High risk suicidal veterans, aged 18-55 years	Dialectical Behavioral Therapy (DBT) (*n*=27) versus TAU (*n*=20)	- Columbia–Suicide Severity Rating Scale[50] - 12 months	No significant difference between DBT and control group (*d*=-0.322, CI -1.146; 0.503, *p*=.444).
Bryan et al., 2017[58]	RCT (1b)	- 72 participants in one military medical clinic (Admitted GHP) - USA	Active duty U.S. Army Soldiers, aged 18+ with suicidal ideation or attempt	Crisis Response Planning standard (CRP-s) (*n*=23) and Crisis Response Planning enhanced (CRP-e) (*n*=24) versus Contract for Safety (CfS) (*n*=25)	- Suicide Attempt Self-Injury Interview[46] - 6 months	No significant difference between CRP and control group (*d*=-0.740, CI -1.567; 0.088, *p*=.080).
Miller et al., 2017[49]	PP (2c)	- 1,376 participants in 8 hospital ED's (ED) - USA	Adults with recent suicide attempt or ideation presented to hospital ED	Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) + Screening (*n*=502) or Screening alone (*n*=377) versus TAU (*n*=497)	- Columbia Suicide Severity Rating Scale[50] + medical records - 12 months	No significant difference between ED-SAFE and control group (*d*=-0.156, CI -0.326; 0.014, *p*=.072).

Study	Design and level of evidence	Setting (classification), total N and country	Population	Intervention (*n*) and contrast (*n*)	Outcome-assessment and followup time	Effect size
Pearson et al., 2017[51 b]	Cluster-RCT (1b)	- 223,861 participants in the community (Community level) - Sri Lanka	People aged 14 years or older in households living in rural villages	Distribution and promotion of household lockable pesticide storage (*n*=114,168) versus usual practice (*n*=109,693)	- Hospital, community and coroner data - 36 months	No significant difference between the intervention group and the control group.[c]
Multilevel						
Two-level		*N=1,046*				*d=-0.622 (95% CI -1.034; -0.210, p=.003)*
Schilling et al., 2016[59]	Cluster-RCT (1b)	- 1,046 participants in 16 technical high school (Community level) - USA	Ninth grade students in technical high school	Signs of Suicide (SOS) (*n*=650) versus wait list control group (*n*=396)	- Single-item measure from the Youth Risk Behavior Survey[60] - 3 months	Significant less suicide attempts in SOS compared to control group (*d*=-0.622, CI -1.034; -0.210, *p*<.003).

Note: [a] The study of Lahoz et al., 2016 is a 5-year follow-up of the study of Hvid et al., 2011.

[b] The study of Pearson et al., 2017 reported in person-years and was not included in the meta-analysis.

[c] The study of Pearson et al., 2017 was not included in the meta-analysis to suicide attempts; effect size is therefore not provided in the table.

Abbreviations: CCS = case-control study. ED = emergency department. GHP = psychiatric ward in general hospital. OPAC = suicide prevention intervention named Outreach, Problem solving, Adherence, Continuity programme. PS = suicide prevention intervention named Screening by professionals. PP = pre-post design. QPR = suicide prevention intervention named Question, persuade and refer. RCT = randomised controlled trial. SMHI = specialty mental health institution. TAU = treatment as usual. YAM = suicide prevention intervention named Youth aware of mental health programme.

RISK OF BIAS WITHIN STUDIES

The quality ratings of the studies are shown in Table 3. Thirteen studies were randomised studies (RCTs). Two out of 16 studies (12.50%) had a low overall risk of bias, meaning that these studies 'were comparable to a well-performed randomised trial'.[61] Nine studies had a moderate overall risk of bias (56.25%), meaning that these studies 'provided sound evidence for a non-randomised study but cannot be considered comparable to a well-performed randomized trial'.[61] Five studies (31.25%) had a serious overall risk of bias, meaning that these studies 'had some important problems'.[61] No studies showed a critical risk of bias. All studies were considered of sound quality according to the guidelines of the Oxford Centre of Evidence-Based Medicine.[29] Hence, all studies were used in the analyses.

Table 3. Risk of bias within studies

Study	Random-isation	Confound-ing	Selection of participants	Classifi-cation of intervention	Deviation intended intervention	Missing data	Measure-ment of outcomes	Selection reported result	**Overall bias**	Comments
Amadéo et al., 2015[47]	Yes	Low	Low	Low	Low	Moderate	Low	Low	**Moderate**	Two-tailed test in spite of the apparently expected direction of the effect; small sample size; missing data.
Bryan et al., 2017[58]	Yes	Low	Moderate	Low	Moderate	Low	Low	Low	**Moderate**	Small sample size (*N*=97) and delay in interventions due to recruitment suspension (recruitment goal was *N*=360).
Cebrià et al., 2013[54]	No	Serious	Low	Low	Low	Low	Moderate	Low	**Serious**	No information about SH; outcome measure could have been influenced by knowledge of the intervention received in the experimental setting (change in 2008).
Goodman et al., 2016[57]	Yes	Moderate	Low	Low	Low	Serious	Low	Low	**Serious**	A high number of drop-out, no ITT/NTT; no information about SH.
Gysin-Maillart et al., 2016[56]	Yes	Low	Low	Low	Low	Moderate	Low	Low	**Moderate**	Missing data due to drop-out.
Hassanian-Moghaddam et al., 2011[53]	Yes	Low	Low	Low	Low	Low	Low	Low	**Low**	Good quality study.
Hvid et al., 2011[42]	Yes	Low	Low	Moderate	Low	Low	Moderate	Low	**Moderate**	Single-blind study; one catchment area so people might, by chance, know each other or meet in the hospital.
Lahoz et al., 2016[48]	Yes	Low	Low	Low	Low	Low	Low	Low	**Low**	Completed and attempted suicide was taken together as an outcome.
Miller et al., 2017[49]	No	Serious	Low	Low	Low	Low	Low	Moderate	**Serious**	Time might have influenced outcomes, time and site (probably) not in final analysis, no information about validity and reliability measures; possible selection of analysis/covariates.
Mishara et al., 2012[52]	No	Moderate	Serious	Moderate	Low	Moderate	Low	Low	**Serious**	Various interventions in different fields, therefore no clearly defined intervention; no outcome data at follow-up; missing data.
Mousavi et al., 2014[55]	Yes	Low	Low	Moderate	Low	Low	Moderate	Low	**Moderate**	Randomisation after the first interview; randomisation, missing data and assessment of information are not clearly described.

Pearson et al., 2017[51]	Yes	Moderate	Low	Low	Low	Low	Low	Low	**Moderate**	Cluster RCT, although corrected in analyses.
Rudd et al., 2015[45]	Yes	Low	Low	Low	Low	Low	Low	Moderate	**Moderate**	Multiple analyses of the intervention-outcome relationship not registered; no significant effect on Fisher exact (two-tailed); analysis selection is possible.
Schilling et al., 2016[59]	Yes	Moderate	Low	Low	Low	Serious	Moderate	Low	**Serious**	Cluster RCT; only significant demographics were included; proportions of participants not given, but probably contrary; more missing items at pre-test; self-assessment.
Vijayakumar et al., 2011[41]	Yes	Low	Low	Low	Low	Moderate	Moderate	Low	**Moderate**	Some 5-10% lost to follow-up; more missing items in TAU-group which decreases the effect; potential bias in the measurement of outcomes.
Wasserman et al., 2015[43]	Yes	Low	Low	Low	Low	Moderate	Moderate	Low	**Moderate**	Cluster RCT; missing data; self-assessment.

Note: Confounding = pre-intervention bias due to confounding. Selection of participants = pre-intervention bias in the selection of participants into the study. Classification of intervention = at-intervention bias in classification of interventions. Deviation intended intervention = post-intervention bias due to deviations from intended interventions. Missing data = Post-intervention bias due to missing data. Measurement of outcomes = Post-intervention bias in measurement of outcomes. Selection reported result = Post-intervention bias in the selection of the reported result.[61]

Results of individual studies

A total of 16 studies with 252,932 participants were selected for the systematic review. All studies were published in the time period of 2011–2017. Thirteen studies were (cluster) randomised controlled trials (81.3%),[41-43,45,47,48,51,53,55-59] two studies were a pre-post design study (12.5%),[49,52] and one study was a case-controlled design (6.3%).[54] Fourteen interventions evaluated unilevel interventions (87.5%),[41-43,45,47-49,51,53-58] and two evaluated multilevel interventions (two-level: *n*=1, 6.3%[59]; three-level: *n*=1, 6.3%[52]). Two studies reported on the effect of suicide prevention interventions on completed suicides (12.5%),[47,52] seven studies on attempted suicides (43.8%)[53-59] and seven studies reported on both (43.8%).[41-43,45,48,49,51] In five of the 16 studies, the setting was an outpatient specialty mental health institution (31.3%),[42,45,48,56,57] in four studies an emergency department (25.0%)[49,53-55] or a community facility (25.0%) was involved,[43,51,52,59] and in three studies the setting was a psychiatric ward of a general hospital (18.8%).[41,47,58] Nine of 16 studies (56.3%) reported on participants who received treatment in a hospital (emergency room or psychiatric department) after non-fatal suicidal behaviour.[41,42,47-49,53-56] In four studies (25.0%) professional groups, such as soldiers, veterans and police officers, were involved.[45,52,57,58] Participants from the community, such as from schools, were reported in three studies (18.8%).[43,51,59]

Synthesis of results

Overall meta-analysis

The study of Pearson et al., 2017 reported in person-years and this outcome could not be pooled with the outcomes of the other studies. Hence that study was not included in the meta-analysis. A total of 15 studies were included in the meta-analysis, all together reporting 62 suicides and 1006 suicide attempts (participants might have attempted suicide multiple times).

The first meta-analysis established the overall effect of any kind of suicide prevention intervention on combined completed and attempted suicides, here defined as suicidal behaviour. Overall meta-analytic regression for this combined effect showed a significant, albeit moderate effect, with all studies favouring suicide prevention interventions over control conditions. The pooled estimate of effect size was d=-0.495 (95% CI -0.677; -0.313, p<.001). The forest plot is shown in Figure 2.

[Insert Figure 2 as online data supplement]

Figure 2. Forest plot suicidal behaviour

Heterogeneity (Q value) of this combined effect of suicide prevention interventions for all studies taken together was 32 (*df*=16, *p*=.011). The I^2 statistic was 50%, indicating moderate heterogeneity, sufficiently to use a random model to fit the data, which was done in this analysis (Higgins). Because of this Q value and I^2 level of heterogeneity of the combined outcomes, the further analyses were performed separately for completed suicides and attempted suicides.

Completed suicides

For suicide prevention interventions on completed suicides, the pooled estimate was *d*=-0.535 (95% CI -0.898; -0.171, *p*=.004), which is a large, statistically significant effect. This effect is larger than the abovementioned combined effect. Q value for these studies was 6 (*df*=6, *p*=.455). The I^2 statistic was 0%, indicating no heterogeneity. This is a robust effect. The forest plot is shown below.

[Insert Figure 3 about here]

Figure 3. Forest plot of completed suicides

Attempted suicides

For suicide prevention interventions on attempted suicides, the pooled estimate was d=-0.449 (95% CI -0.618; -0.280, p<.001), which is a moderate, statistically significant effect, slightly smaller than the above-mentioned combined effect. The forest plot is shown below. The Q value for these studies was 37 (df=14, p=.001). The I^2 statistic was 62%, indicating large heterogeneity.

[Insert Figure 4 about here]

Figure 4. Forest plot of attempted suicides

ADDITIONAL ANALYSIS

Setting of intervention

In order to establish whether outcomes differ across settings in which suicide prevention intervention is provided, a separate pre-envisioned moderator analysis of studies according to the type of setting was done. Results are shown separately for completed suicides and attempted suicides.

Completed suicides

For completed suicides, suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital show the highest effect: *d*=-1.082 (95% CI -2.027; -0.137, *p*=.025). This is a large effect. Next effective were community-level interventions, with *d*=-0.832 (95% CI -1.406; -0.259, *p*=.004), a large effect size. Emergency room setting suicide prevention interventions had a small, non-significant effect size of *d*=-0.289 (95% CI -1.082; 0.503, *p*=.474). Outpatient specialty mental health setting interventions had a worse outcome for suicide prevention interventions than the control, with an effect size of *d*=0.088 (95% CI -0.655; 0.831, *p*=.817); this effect was not significant. With the use of a random effects model, Q between groups was 5 (*df*=3, *p*=.145).

Attempted suicides

For attempted suicides, outpatient specialty mental health setting interventions showed the highest effect: *d*=-0.705 (95% CI -1.275; -0.135, *p*=.015). This is a large effect. Next best were suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital, with *d*=-0.483 (95% CI -0.892; -0.073, *p*=.021), a moderate effect size. Community-level interventions had an effect size of *d*=-0.324 (95% CI 0.513; -0.136, *p*=.001) and emergency room setting suicide prevention interventions had an effect size of *d*=-0.319 (95% CI -0.528; -0.110, *p*=.003). Both were small effects. With the use of a random effects model, Q between groups was 2 (*df*=3, *p*=.565).

Multilevel suicide prevention interventions

Suicide interventions were labelled as multilevel if they contained elements that were performed in different healthcare settings or domains and by different providers. Effect sizes in terms of completed suicides differed for multilevel interventions from non-multilevel interventions as follows: non-multilevel intervention effects were: *d*=-0.334 (95% CI -

0.804;0.136, *p*=.163) which was a small and non-significant effect. Multilevel interventions were: *d*=-0.832 (95% CI -1.406; -0.259, *p*=.004), which is a large, significant effect. Q between groups was 2 (*df*=1, *p*=.188). Effect sizes in terms of attempted suicides differed for multilevel interventions from non-multilevel interventions as follows: non-multilevel interventions: *d*=-0.443 (95% CI -0.632; -0.254, *p*<.001), which was a moderate and significant effect. Multilevel interventions were: *d*=-0.622 (95% CI -1.034; -0.210, *p*=.003) which was a large, significant effect. Q between groups was 0.598 (*df*=1, *p*=.438).

Synergistic effect

The meta-regression analysis examined whether a synergistic effect for multilevel suicide prevention interventions could be found on combined outcomes. The analysis showed a significant effect of the number of levels in the suicide prevention intervention on effect size (*Q*=4.591, *df*=1 *p*=.032). With single-level interventions, the effect size was -0.3, which is a small effect. Two-level interventions show an effect size of approximately -0.5, which is moderate, and three levels show a large effect, going up to -0.8, as can be seen in Figure 5.

[Insert Figure 5 about here]

Figure 5. Meta-regression of number of intervention levels on the standardised mean difference

RISK OF BIAS

Risk of bias within studies: meta-regression

As indicated on the Risk of Bias (ROB; Table 3), ROB varied greatly; moreover, there were a substantial number of studies with serious ROB. Hence, a meta-regression was performed to explore whether the level of ROB in the studies was associated with the effect as found in the analysis. The analysis showed that there was no significant association (Q =0.033, df=1 p=.855). Hence, all studies could be used for the analysis, as was done in this study.

Risk of bias across studies: publication bias

A test for publication bias was performed. The Begg funnel plot with observed and imputed studies is shown in Figure 6. It shows that the adjusted estimate is fairly close to the original. The Egger test was not significant, indicating symmetry (t(17)=1.620, 95% CI: -2.21; 0.29, p=.124). This indicates that no significant publication bias seems to be the case, and the reported effect is valid.

[Insert Figure 6 as Online data supplement]

Figure 6. Funnel plot

Discussion

The aim of this review was to evaluate the effectiveness of suicide prevention interventions in different settings, to compare their relative effectiveness by providing an estimate of their effect size, and to explore possible synergism of multilevel interventions in a meta-analysis. This systematic review includes 252,932 participants in 16 controlled studies. The meta-analysis, for the first time, provides a comparative estimate for the effect of different types of suicide prevention interventions, based on 15 controlled studies, with 29,071 participants in various settings. The findings show that suicide prevention interventions are effective in

preventing both completed and attempted suicides. The effect size for completed suicides is larger than for attempted suicides. It might seem counterintuitive that interventions effective against completed suicides do not always prevent suicide attempts, as the greatest risk of completed suicide are suicide attempts. However, a possible explanation might be that the profile of the patient group that attempts suicide may differ in terms of personality disorder or method of suicide. Therefore, it might be that a suicide prevention intervention that is effective against one is not automatically as effective against the other outcome. This may be related to findings that people who complete suicide, in comparison to people who attempt suicide, are more often middle- or elderly-aged men,[62,63] and choose lethal means – such as hanging – more frequently as the suicide method[62]. People who attempt suicide are more often younger women,[62] and use less lethal means – such as overdose or cutting – as suicide method.[62] More research is needed to whether individuals that complete versus attempt suicide differ with regards to the presence of psychiatric disorders.

Differences between completed suicides and attempted suicides can also be identified in terms of intervention settings. For completed suicides, suicide prevention interventions for patients admitted to a psychiatric ward in a general hospital and community-level interventions showed large effects. Interventions in other settings showed no significant effect. However, in attempted suicides, suicide prevention interventions delivered in outpatient specialty mental health settings showed a large effect and, for patients admitted to a psychiatric ward in a general hospital, a moderate effect. Community level and emergency room-based interventions had only small effects. It is remarkable that, although an intervention provided in an outpatient specialty mental health institution might be very effective in preventing suicide attempts, it might not at all be effective in preventing completed suicides. A very tentative explanation is that there are different patient profiles: a) patients who require an admission to advert suicide, and b) patients whose suicidal thoughts

and behaviour might be related to a personality disorder or coping problems and who might benefit more from outpatient treatment. In the latter group, patients might be more amenable to interventions that foster individual autonomy. This finding is of high clinical and policy relevance as, until now, the general assumption in research has been that the interventions will work equally for both outcomes. It underscores the need to be able to discern risk for completed suicide from risk for attempted suicide in clinical practice. However, making such determinations remains a substantial clinical challenge.

The findings also show that multilevel interventions are more effective than single level interventions and, further, that effect size rises significantly with the number of levels involved. Regarding synergism, a synergistic effect of multilevel interventions would ideally occur when the combined effect of the interventions is greater than the sum of the individual effects. This could be expressed as an exponential relationship between the numbers of intervention levels. In this study, a more linear relationship was found. However, as the effect sizes were considerable, ranging from -0.3 to -0.5 and -0.8 for the three-level intervention, a ceiling effect might have occurred. Although this does not yet provide direct evidence for synergism as described above, the findings are promising. In view of the low number of studies with more than one level, further research into multilevel interventions is recommended. Due to the added value of multilevel interventions and the synergistic potential, we recommend the implementation of multilevel suicide prevention interventions above one level.

STRENGTHS AND LIMITATIONS

This study is the first to perform a systematic review and meta-analysis evaluating controlled studies examining the effect of any kind of suicide prevention intervention and providing an estimate of the effect size. The number of participants was high, 252,932, and the focus on

quantitative outcomes for completed and attempted suicides enabled us to establish clear outcomes of high societal relevance. Moreover, despite completed suicides being a very low base rate behavior, we found significant results which is probably due to the very large number of patients that were included in our study. There were no indications for publication bias, and it is not expected that relevant studies were excluded or missed in the review process since the authors consulted multiple sources for the identification of studies. With regard to limitations, we compared the three intervention conditions that were examined in the Wasserman et al. (2015) study[43] separately, with the one control condition of their study for the meta-analysis, rather than comparing the three interventions together with the control condition. This was done to prevent the loss of relevant information, as there were differences in the interventions themselves and, importantly, also in their effectiveness in the prevention of suicide. A second limitation is that we only included two multilevel interventions in the meta-analysis of which one was a two-level intervention and one was a three-level intervention. Multilevel interventions should, therefore, be the focus of further research, as the current evidence indicates a greater effect of multilevel interventions compared to unilevel interventions and synergistic potential. Moreover, completed suicides remain a low base rate behavior. This resulted in our study in a less precise estimate of the effect, compared to suicide attempts. It is desirable for future research that more studies will examine the effect of suicide prevention interventions on preventing completed suicide, as more studies will enable more precise estimates of the effects.

FUTURE RESEARCH

Although the number of participants in this review was high (*N*=252,932), and the number included in the meta-analysis as well (N=29,071), the number of controlled studies reporting on completed or attempted suicides identified in this study (*N*=16) was lower than expected in

view of the globally rising suicide rates and the 2013 commitment of the World Health Organisation Member States for the development of suicide prevention interventions. Many studies are non-controlled investigations that report on indirect precursors of suicide such as suicidal ideation. This might be due to the fact that suicide is a statistically rare event; however, preventing suicide should be the ultimate goal of a suicide prevention intervention. We, therefore, recommend future research with controlled designs to further examine the effectiveness of suicide prevention interventions – especially multilevel interventions – on numbers of completed or attempted suicides. Future research should also examine further differential effects across outcomes and across specific characteristics of settings. For example, for some people, a psychiatric admission might be very effective in preventing suicidal behaviours, while for others it might cause pervasive distress.[64] Also, some settings may have more effect on prevention of completed suicides, while others may be more effective for attempted suicides. More insight is needed into which characteristics contribute to making an intervention in a particular setting more or less effective, and in which respect. This study shows that the assumption that interventions have the same effect on completed and attempted suicides, and in different settings, is no longer valid. A related recommendation for future research would be to determine optimal strategies for professionals to discern risk for completed suicide from risk for an attempt, as appropriate interventions for each may differ. Finally, further research is needed to explore and further improve synergism in multilevel interventions.

CONCLUSION

Suicide prevention interventions are effective in preventing suicidal behavior and should be widely implemented. The findings suggest that clinicians should make an assessment of whether their patient is at serious risk for completing suicide. This will assist in determining

the most appropriate treatment: intervention provided in the psychiatric ward of a general hospital or, alternatively, prevention of attempted suicide in an outpatient specialty mental health clinic. Moreover, multilevel interventions should be the focus of further research due to a greater effect and synergistic potential.

Contributors

X and X designed the study. X, X and X performed the systematic review and data extraction. X and X assessed the risk of bias of individual studies. X performed the meta-analysis. X and X wrote the first draft of the paper, and X, X, X, X, and X contributed in the process of drafting and revising. All authors gave their agreement and approval for all aspects of the final version of the paper.

Declaration of interests and funding

The authors declare no competing interests. The authors of this study had full access to all the data in the study and had final responsibility for the integrity of the data, the accuracy of data analysis and the decision to submit for publication. This research was funded by the Netherlands Organisation for Health Research and Development, grant number X. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Appendix 1: PRISMA Checklist

Section/topic	#	Checklist item	Page
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	0
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2)	8

		for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	19
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	19
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	24
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	21
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policymakers).	24
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	26
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	28
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	29

Appendix 2: Search strategy

PubMed

#1 Systematic reviews

(‘suicide’[MeSH Terms] OR ‘suicide’[All Fields]) AND (‘prevention and control’[Subheading] OR (‘prevention’[All Fields] AND ‘control’[All Fields]) OR ‘prevention and control’[All Fields] OR ‘prevention’[All Fields]) AND (‘methods’[MeSH Terms] OR ‘methods’[All Fields] OR ‘intervention’[All Fields]) AND (‘review’[Publication Type] OR ‘review literature as topic’[MeSH Terms] OR ‘systematic review’[All Fields]) AND (‘2011/01/01’[PDAT] : ‘2017/12/15’[PDAT])

#2 Clinical trials

(‘suicide’[MeSH Terms] OR ‘suicide’[All Fields]) AND (‘prevention and control’[Subheading] OR (‘prevention’[All Fields] AND ‘control’[All Fields]) OR ‘prevention and control’[All Fields] OR ‘prevention’[All Fields]) AND (‘methods’[MeSH Terms] OR ‘methods’[All Fields] OR ‘intervention’[All Fields]) AND (‘clinical trial’[Publication Type] OR ‘clinical trials as topic’[MeSH Terms] OR ‘clinical trial’[All Fields]) AND (‘2011/01/01’[PDAT] : ‘2017/12/15’[PDAT])

The PubMed search strategy for systematic reviews and clinical trials was also translated for the PsycINFO and Cochrane databases.

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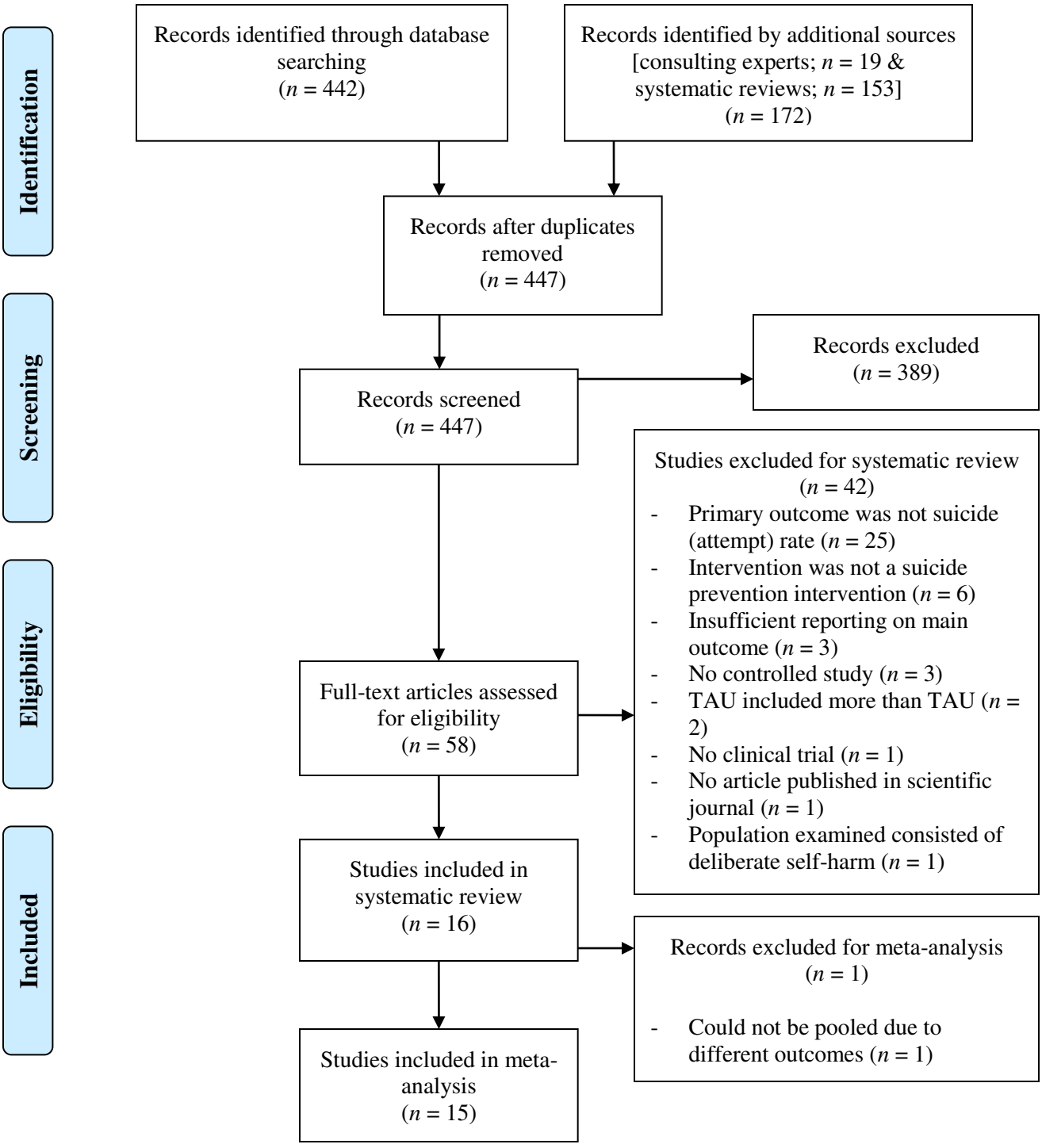
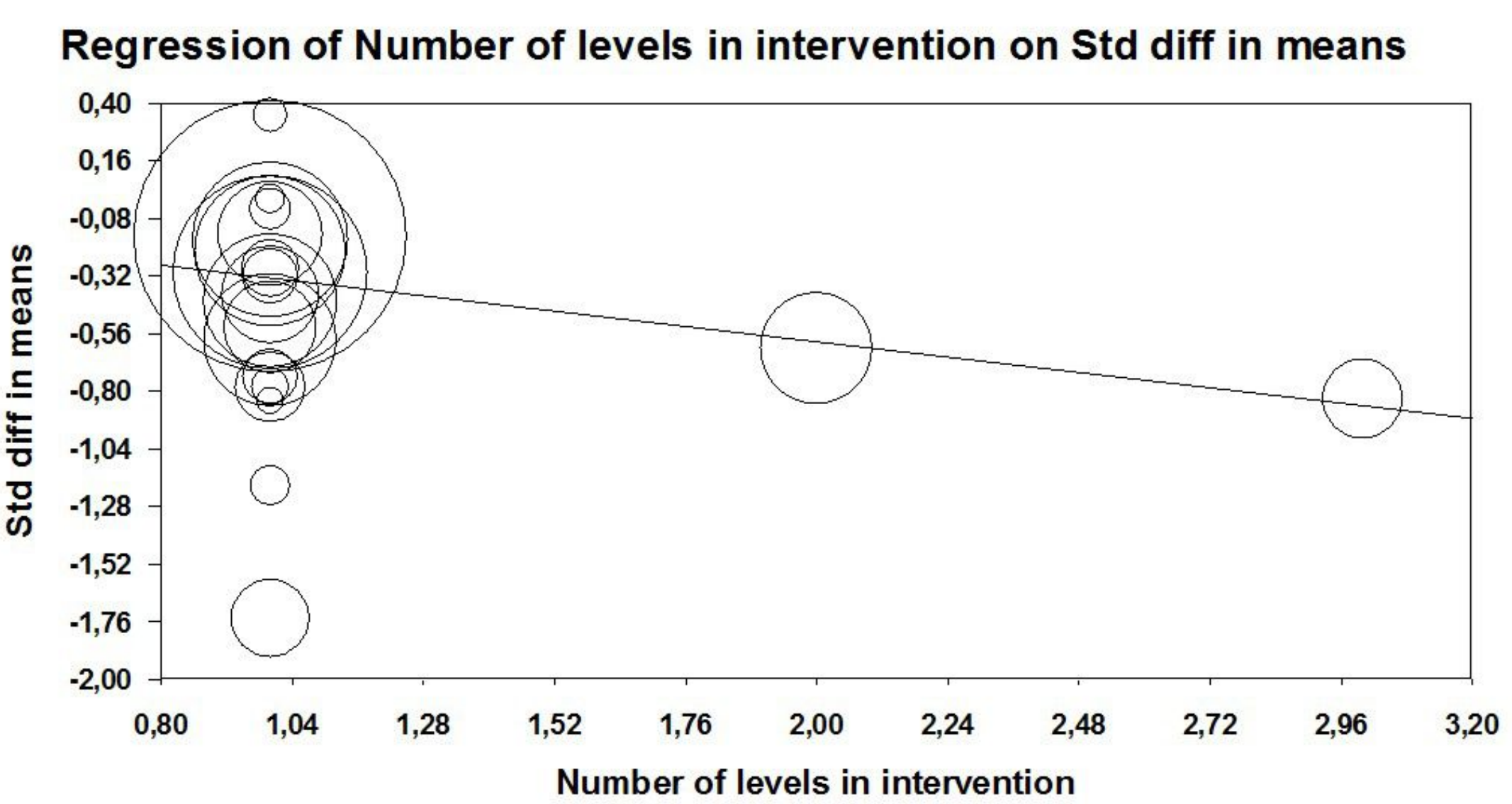
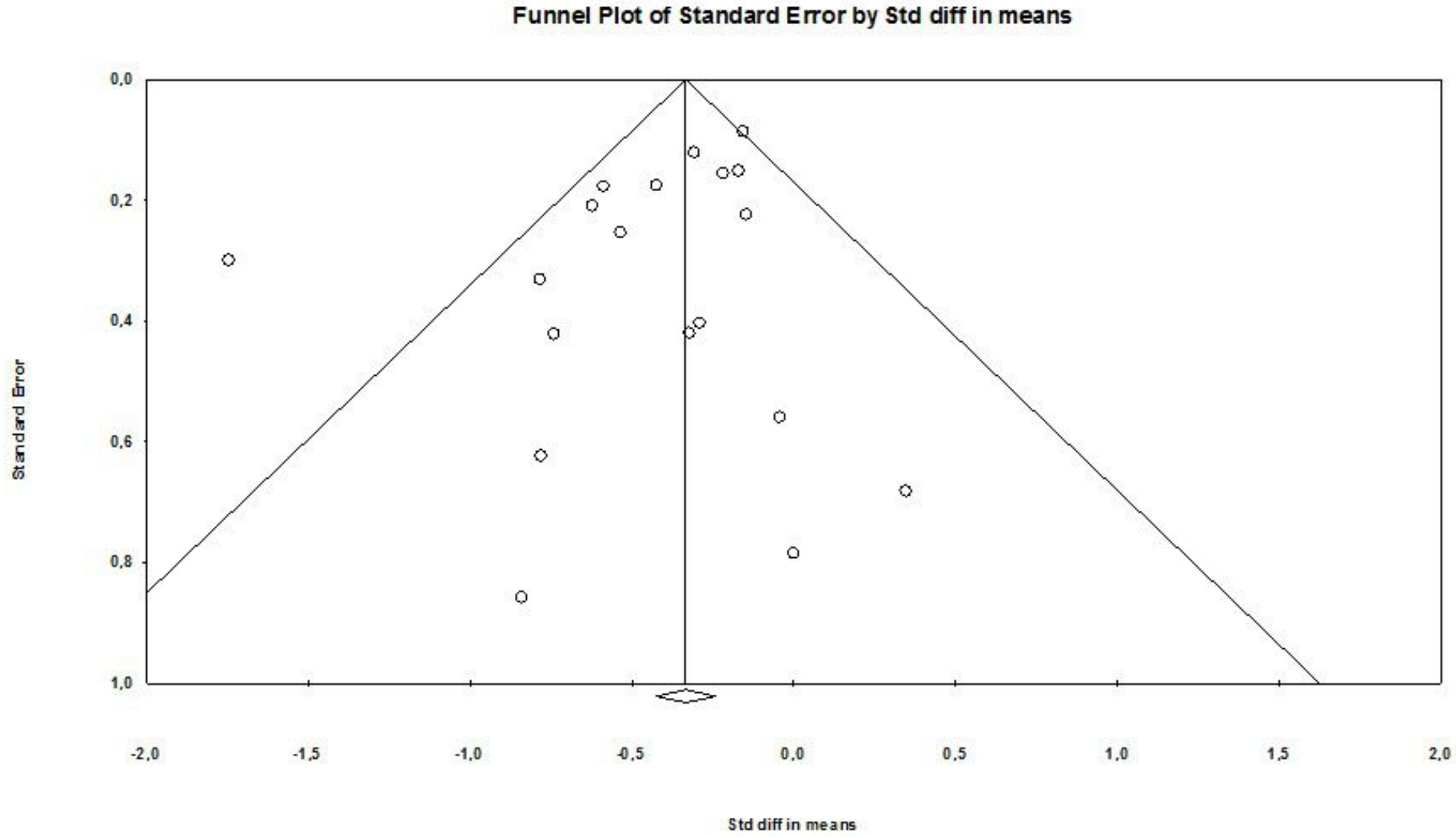

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 442)
Records identified by additional sources [consulting experts; n = 19 & systematic reviews; n = 153] (n = 172)
Records after duplicates removed (n = 447)
Records screened (n = 447)
Records excluded (n = 389)
Full-text articles assessed for eligibility (n = 58)
Studies excluded for systematic review (n = 42)
- Primary outcome was not suicide (attempt) rate (n = 25)
- Intervention was not a suicide prevention intervention (n = 6)
- Insufficient reporting on main outcome (n = 3)
- No controlled study (n = 3)
- TAU included more than TAU (n = 2)
- No clinical trial (n = 1)
- No article published in scientific journal (n = 1)
- Population examined consisted of deliberate self-harm (n = 1)
Studies included in systematic review (n = 16)
Records excluded for meta-analysis (n = 1)
- Could not be pooled due to different outcomes (n = 1)
Studies included in meta-analysis (n = 15)


Regression of Number of levels in intervention on Std diff in means
Std diff in means
0,40
0,16
-0,08
-0,32
-0,56
-0,80
-1,04
-1,28
-1,52
-1,76
-2,00
0,80
1,04
1,28
1,52
1,76
2,00
2,24
2,48
2,72
2,96
3,20
Number of levels in intervention


Funnel Plot of Standard Error by Std diff in means
Standard Error
0,0
0,2
0,4
0,6
0,8
1,0
-2,0
-1,5
-1,0
-0,5
0,0
0,5
1,0
1,5
2,0
Std diff in means