Characteristics and predictors of suicidality in young people with clinical depression: a systematic review protocol

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ABSTRACT

Objective: The objective of this review is to examine clinical, psychosocial, and biological factors associated with suicidality in young people diagnosed with depression. This review will describe risk and protective factors, focusing on modifiable attributes, in order to inform suicide prevention and early intervention strategies.

Introduction: Suicide is the world’s second-leading cause of death among young people. Depression is closely associated with suicide; however, it lacks specificity as a predictor of suicidal behavior. There is a clear need to improve our understanding of both risk and protective factors associated with the full spectrum of suicidality in young people, across a range of depressive disorders.

Inclusion criteria: Studies that include young people 15 to 25 years of age with a diagnosis of depression made in accordance with a diagnostic classification standard will be considered. Diagnosis must be made using a structured clinical interview or be received through standard clinical practice. Analytical cross-sectional studies, prospective and retrospective cohort studies, and case-control studies will be included. Studies must include an assessment of suicidality made using standardized or non-standardized tools. A broad range of inpatient and outpatient settings will be considered.

Methods: MEDLINE, Embase, and PsycINFO will be searched for studies published in English, with no date limitation. Two independent reviewers will conduct study screening, assess methodological quality, and extract data using standardized tools. If there is sufficient homogeneity across studies, meta-analyses using a random-effects model will be conducted. If quantitative meta-analysis is not possible, a narrative synthesis will be undertaken.

Systematic review registration number: PROSPERO CRD42020151612.

Keywords: adolescent; depression; early intervention; suicide; youth


Introduction

The period of mid-adolescence to young adulthood is a particularly vulnerable period for the onset of mental disorders and for suicide. Globally, suicide is the second-leading cause of death for people 15 to 29 years of age.1 Completed suicide represents the extreme end of a spectrum of suicidality. In this review, suicidality will be defined as the full spectrum of suicidal thoughts (encompassing passive and active thoughts of death), suicidal behavior (including preparatory suicidal acts and suicide attempt), and completed suicide.2-4 Suicide deaths are preventable5; however, suicide is a complex phenomenon and no single approach to prevention is likely to be universally effective.6 Young people who experience suicidal thoughts or behaviors comprise a heterogeneous group7 and suicide is difficult to predict at the individual level.8,9 Numerous factors are associated with increased risk of completed suicide in young people, including affective disorders, substance use, family adversity, non-heterosexual orientation, suicidal ideation, and prior suicidal attempt.2,8,10 With the possible
exception of suicide attempt, these risk factors lack specificity and are not reliable predictors of suicide at an individual level.\(^5\) \(^1\) \(^1\) A recent meta-analysis found that even suicidal ideation, often suggested as a strong predictor for future suicidal behavior, has a low positive predictive value for later suicide.\(^1\) In the meta-analysis, the positive predictive value across 58 psychiatric cohorts was 3.9% (95% confidence interval, 2.2% to 6.6%), suggesting that ideation has limited clinical utility as a suicide predictor.\(^1\) In part, this is due to the relatively low base rate of completed suicide, even among psychiatric cohorts of young people.

As completed suicide is a relatively infrequent outcome, the predictive validity of suicide measures is somewhat limited.\(^9\) \(^13\) \(^14\) Evidence shows that no individual instrument or pooled subgroups of instruments are able to classify individuals as being at risk of suicide with a level of accuracy necessary to be clinically useful.\(^1\) Considering the existing shortcomings in our ability to predict suicide in young people, there is a clear need to consider the full spectrum of suicidality\(^2\) \(^3\) in order to develop a better understanding of factors associated with the development of trajectories that lead to completed suicide.\(^8\) Also, the burden associated with non-fatal suicide attempts is substantial, due to psychosocial morbidity, secondary psychological distress, lost productivity, and increased use of health services.\(^16\) It is therefore important to consider the entire spectrum of suicidality, not only suicide deaths.

Young people with depression are an ideal group to consider when exploring these concepts. Depression is the most common feature among young people who experience suicidality,\(^17\) \(^18\) yet it lacks specificity as a predictor of suicidal behavior.\(^5\) Although thoughts of suicide are prevalent among people with depression, it is difficult to predict whether a particular young person with depression will actually attempt suicide.\(^1\) \(^2\) \(^12\) \(^19\) This poor predictive ability means that it is imperative to improve our understanding of which specific characteristics are associated with the full spectrum of suicidality, as well as factors that are protective against suicide. Suicidal behavior often co-occurs with other health risk behaviors such as substance use and deliberate self-harm.\(^2\) \(^8\) Investigating associations between such behaviors and suicidality is essential to improving our understanding of the suicidal process in young people with depression. There is an abundance of primary studies investigating suicidality in young people with depression\(^4\) \(^7\) \(^10\) \(^13\) across a wide variety of settings, providing a rich source of data to review.

To identify prior systematic reviews in this area, a scoping search was conducted in the Cochrane Database of Systematic Reviews, MEDLINE, PROSPERO, the Database of Abstracts of Reviews of Effects (DARE), and the JBI Database of Systematic Reviews and Implementation Reports. While there are previously published systematic reviews of suicide interventions, prevention efforts, screening methods, or specific etiological factors, there are no comprehensive systematic reviews specifically characterizing suicidality in the proposed review’s target population of young people with clinically diagnosed depressive disorders. Also, the majority of existing reviews focus on suicide in non-clinical samples of young people.

The aim of this proposed review is to characterize suicidality in young people with a range of clinically diagnosed depressive disorders by examining clinical, psychosocial, and biological factors associated with suicidality in this at-risk cohort. We will describe both cross-sectional and longitudinal predictors of suicidality. Factors that are associated with increased risk of suicidality (ie, risk factors) and those associated with decreased risk of suicidality (ie, protective factors) will be explored. A key focus will be to identify modifiable factors (ie, factors that are amendable to change) in order to inform suicide prevention and early intervention strategies.

**Review question**

What clinical, psychosocial, and biological risk and protective factors are associated with suicidal thoughts and behaviors (encompassing passive and active thoughts of death, preparatory suicidal acts, suicide attempt, and completed suicide) in young people with depression, and do these risk factors vary across settings?

**Inclusion criteria**

**Participants**

This review will examine studies that include participants 15 to 25 years of age with a current or lifetime diagnosis of any depressive disorder. Studies including participants younger than 15 years or older than 25 years will also be included if relevant data for participants within the 15 to 25 year age range are presented separately to data from other
participants. Diagnosis of a depressive disorder must be made on the basis of a structured clinical interview or be received through standard clinical practice in an inpatient or outpatient setting. Participants with any type of unipolar or bipolar depressive disorder will be included, as previous research has shown no distinction between depressive diagnoses with regard to the frequency and severity of suicidality. Diagnoses will include major depressive disorder, dysthymia, bipolar disorder (I and II), cyclothymic disorder, seasonal affective disorder, and any other depressive disorder diagnosis made in accordance with a diagnostic classification standard (ie, either the WHO International Classification of Diseases or the Diagnostic and Statistical Manual of Mental Disorders). The diagnosis of a depressive disorder may be the primary diagnosis or a secondary diagnosis. Considering the relatively high rates of psychiatric comorbidity in depression and extensive evidence suggesting the high prevalence of comorbid disorders in young people who attempt suicide, studies including participants with comorbid psychiatric disorders or personality disorders will not be excluded. Studies must also encompass an assessment of suicidality that occurs in conjunction with a diagnosed depressive disorder. There will be no restriction on the length of study duration or follow-up period.

**Outcomes**
The outcome of interest is suicidality, encompassing the full spectrum of suicidal thoughts (encompassing passive and active thoughts of death), suicidal behavior (including preparatory suicidal acts and suicide attempt), and completed suicide. Thoughts and behaviors may be a single episode or recurrent. Assessment of suicidality may be made using standardized or non-standardized tools, which can be either self-reported or clinician-administered measures. Assessments of depression and suicidality must occur at the same time or be made in reference to the same time period.

**Types of studies**
A range of observational study designs will be included, encompassing analytical cross-sectional studies, prospective and retrospective cohort studies, case-control studies, and case series. As this review is concerned with issues of etiology and risk, rather than intervention effectiveness, experimental studies such as randomized controlled trials will be included only if pre-intervention data can be extracted from the publication. Case reports, conference abstracts, letters, editorials, and purely qualitative studies will be excluded. Only articles published in peer-reviewed academic journals will be included. The decision to limit the review to peer-reviewed journals was made due to resource constraints. In an attempt to capture the highest-quality source material for the review, the authors have elected to focus on peer-reviewed journals only in order to best utilize the resources available to conduct the review. No restrictions will be placed on the country in which the study was conducted in order to include findings from a diverse range of health care settings across low-, middle-, and upper-income countries.

**Methods**
This systematic review protocol has been developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement and the proposed review will follow the JBI methodology for systematic
reviews of etiology and risk. The protocol was registered with PROSPERO (CRD42020151612).

Search strategy
An initial search of MEDLINE (Ovid) was undertaken to identify articles pertaining to suicide in young people with depression. Keywords in the titles and abstracts of relevant articles, and the index terms used to describe the articles, were used to develop a preliminary search string. This was constructed using Medical Subject Headings (MeSH terms) related to suicide and depression in young people. MeSH terms were identified using the US National Library of Medicine (NLM) “MeSH on Demand” tool, and further refined using the NLM MeSH Browser database to map relevant keywords onto the MeSH tree structure. Expanded MeSH terms are also included in the search string as free text and will be searched for in the title, abstract, subject heading word, floating sub-heading, and keyword heading word fields in MEDLINE. An example search strategy for MEDLINE (Ovid) is included in Appendix I.

MEDLINE, Embase, and PsycINFO databases, all using the Ovid platform, will be included in the final search. The search string will be adapted as necessary to the syntax and subject headings of each database. Where necessary, truncation and wildcards will be used to account for abbreviations and differences in UK and US spelling conventions and terminology. No upper or lower limitations will be placed on date of publication. Articles published in English will be included. The search process will be conducted twice: an initial search to identify records for screening, followed by a second search conducted immediately prior to the final analysis to identify any new articles published since the initial search. The reference lists of all included studies will also be screened for any additional studies.

Study selection
After performing the primary searches, the Ovid multifile search function will be used to de-duplicate records across the three databases. This de-duplicated set of records will be exported to Covidence (Veritas Health Innovation, Melbourne, Australia). A second de-duplication of records will then be conducted within Covidence. A two-step screening process will be employed. Initially, two review authors will independently screen titles and abstracts of all publications against the inclusion criteria. If a selection decision cannot be made on the basis of the abstract alone, the record will be retained for full-text screening. At the second screening stage, the full text of all publications included at the first screening stage will be independently screened by two review authors to determine eligibility. If a publication contains insufficient information to make a decision in accordance with the inclusion criteria, the lead review author will attempt to contact the publication’s lead author by email to obtain the required information.

If the full-text of a publication is not available through the relevant journal website or journal repository, all possible alternative avenues of obtaining a copy of the publication will be explored, such as ResearchGate, Google Scholar, or through inter-library loan. If necessary, the lead review author will attempt to contact the publication’s lead author by email to obtain a full-text copy of the publication. If these attempts are unsuccessful, the publication will be excluded from review. Any publications excluded in this way will be listed in an appendix.

Inclusion and exclusion decisions at each stage will be recorded by each reviewer in Covidence. In the case of a disagreement between reviewers, a consensus decision will be made through consultation between reviewers. There will be no process of blinding review authors to any aspect of the citation details, such as author names or institutions. The process of selection will be comprehensively reported using the PRISMA flow diagram framework.

Assessment of methodological quality
Methodological quality will be assessed by two independent reviewers using standardized critical appraisal instruments from JBI for cohort studies, case-control studies, case series, and analytical cross-sectional studies. If any randomized controlled trials are included in the review, these will be assessed using JBI critical appraisal tools for cohort studies or case-control studies, as aspects relating to interventions are not within scope of this review. Randomized controlled trials will only be included if pre-intervention data can be extracted from the publication. JBI critical appraisal tools incorporate critical evaluation of numerous important aspects, including sampling strategy, sample representativeness, identification of and adjustment for confounding factors, reliability and validity of outcome assessment methods, and incomplete reporting.
Any disagreements between reviewers will be resolved through discussion or by consultation with a third reviewer. Results of the critical appraisal process will be reported in narrative and tabular form. Data will be extracted from all studies (wherever possible), regardless of methodological quality. Results of the critical appraisal process will be used to inform the analysis and interpretation of results.

**Data extraction**
At least two reviewers will independently extract data from all included studies using Covidence. A standardized data extraction form will be created in accordance with the JBI data extraction methodology for systematic reviews of etiology and risk. Data extraction fields will include characteristics of the publication, characteristics of the study design and setting, characteristics of the study population and recruitment methodology, exposures of interest, suicidality outcomes and assessment measures, analytical measures employed, results, and effect sizes. In the case of any discrepancies in extracted data between reviewers, a consensus decision will be made through consultation between reviewers and the involvement of a third reviewer, if necessary. In the case of missing data, the lead review author will attempt to contact the publication author by email.

**Data synthesis**
Where possible, data will be pooled across studies in a random-effects meta-analysis using R software (R Foundation for Statistical Computing, Vienna, Austria). Effect sizes will be expressed as relative risk ratios for dichotomous data and Hedges g for continuous data, along with their corresponding 95% confidence intervals. Use of a random-effects model is based on the assumption that there is likely to be variability in the data arising from within and between study samples. This variability is likely to encompass variations with respect to important attributes such as demographic variables, depression characteristics, and suicidality assessment methods. To allow for uncertainty in the estimation of $\tau^2$, a Bayesian approach will be adopted as the primary model; however, the results will be presented using other models in a sensitivity analysis. It is expected that many studies will present suicidal outcomes in terms of dichotomous variables, such as “completed vs non-completed suicide” or “any suicidality vs no suicidality”; a Bayesian approach lends itself to meta-analysis of binary outcome data. Heterogeneity will be assessed through visual inspection of the meta-analysis output (ie, forest plot) and calculation of $\chi^2$ and $I^2$ statistics. If there is statistically significant heterogeneity across studies, a narrative synthesis will be undertaken to describe included studies and their findings. The narrative synthesis will be presented in accordance with the JBI framework for systematic reviews of etiology and risk.

Subgroup analyses will be conducted, where possible. Studies will be grouped based on relevant attributes of study design, participant characteristics, or exposures. Wherever possible, populations will be grouped and compared on the basis of key attributes of interest such as age of depression onset, type of diagnostic method (eg, structured interview/standard clinical practice), type of depression diagnosis (eg, unipolar/bipolar), and comorbid diagnosis (eg, substance use disorder, personality disorders, psychotic disorders). Textual summaries of key outcomes of the studies within each group will be produced, comparing similarities and differences between characteristics and outcomes among studies within each group. Characteristics of studies and extracted data will also be presented in tables and figures.

**Assessing certainty in the findings**
Quality of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. It is anticipated that the following outcomes will be included in a summary of findings table incorporating GRADE ratings: passive and active thoughts of death, preparatory suicidal acts, suicide attempt, and completed suicide.

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**References**


## Appendix I: Search strategy

### MEDLINE (Ovid)
Search conducted 16 April 2020

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<td>exp suicide/</td>
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