BMJ Open

Psychosocial interventions for the prevention of self-harm repetition: protocol for a systematic review and network meta-analysis

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To cite: Orri M, Gifuni AJ, Ougrin D, *et al*. Psychosocial interventions for the prevention of self-harm repetition: protocol for a systematic review and network meta-analysis. *BMJ Open* 2023;**13**:e072289. doi:10.1136/bmjopen-2023-072289

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-072289).

Received 01 February 2023
Accepted 03 August 2023

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ABSTRACT

Introduction Suicide is an important public health problem. Providing evidence-based psychosocial interventions to individuals presenting with self-harm is recognised as an important suicide prevention strategy. Therefore, it is crucial to understand which intervention is most effective in preventing self-harm repetition. We will evaluate the comparative efficacy of psychosocial interventions for the prevention of self-harm in adults.

Methods and analysis We will perform a systematic review and network meta-analysis (NMA) of randomised controlled trials (RCTs) testing psychosocial interventions for the prevention of self-harm repetition. We will include RCTs in adults (mean age: 18 years or more) who presented with self-harm in the 6 months preceding enrolment in the trial. Interventions will be categorised according to their similarities and underpinning theoretical approaches (eg, cognitive behavioural therapy, case management). A health sciences librarian will update and adapt the search strategy from the most recent Cochrane pairwise systematic review on this topic. The searches will be performed in MEDLINE (Ovid), Embase (Ovid), PsycInfo (Ovid), CINAHL (EBSCO), Cochrane Central (Wiley), Cochrane Protocols (Wiley), LILACS and PSYNDEX from 1 July 2020 (Cochrane review last search date) to 1 September 2023. The primary efficacy outcome will be self-harm repetition. Secondary outcomes will include suicide mortality, suicidal ideation and depressive symptoms. Retention in treatment (ie, drop-outs rates) will be analysed as the main acceptability outcome. Two reviewers will independently assess the study eligibility and risk of bias (using RoB-2). An NMA will be performed to synthesise all direct and indirect comparisons. Ranked forest plots and Vitruvian plots will be used to represent graphically the results of the NMA. Credibility of network estimates will be evaluated using Confidence in NMA (CINeMA).

Ethics and dissemination As this is the protocol for an aggregate-data level NMA, ethical approval will not be required. Results will be disseminated at national/international conferences and in peer-review journals.

Trial registration number CRD42021273057.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Network meta-analysis (NMA) allows the simultaneous comparison of multiple interventions in a single model.
⇒ NMA maximises the use of available evidence by using both direct and indirect comparisons among interventions, thus improving precision of intervention effect estimates.
⇒ NMA provides a ranking of the interventions according to their effectiveness.
⇒ A potential limitation is violating the transitivity assumption for the indirect comparisons in the network, which can impact the validity of the NMA results. In case violation of the transitivity assumption is detected, reasons for lack of transitivity will be explored in subgroup analyses.
⇒ As in traditional meta-analyses of psychosocial interventions, publication bias, selective/incomplete reporting, study quality and challenges inherent to blinding in clinical trials of psychosocial interventions can affect the validity of the results.

INTRODUCTION

Suicide and self-harm is an important cause of morbidity and mortality worldwide, and its prevention is of paramount importance.[1 2] According to the WHO, the global burden of suicide is estimated at 700 000 deaths each year (10.6 per 100 000 individuals, all ages combined)[3 4] and is considered to be underestimated. The rate of non-fatal self-harm (defined as any type of self-injury or self-poisoning regardless of the suicidal intent; hereafter referred to as *self-harm*[5]) is considerably higher, with more than 500 000[6] and 200 000[7] people presenting to emergency departments for self-harm in the US and the UK, respectively.

Evidence shows that self-harm is highly lethal in adults, with more than half of those

who attempt suicide (defined as self-harm behaviour with intent to die) dying at the first attempt.[8 9] When non-lethal, self-harm carries an elevated risk of subsequently repeating self-harm and dying by suicide, as well as to experience negative psychosocial and economic consequences.[2 10] Meta-analytic evidence shows that 15%–25% of individuals who presented to hospitals with self-harm repeated the behaviour within a year.[11] Furthermore, a recent meta-analysis reported that the risk of suicide mortality after emergency department contact for self-harm was 2.8% at 1 year, 5.6% at 5 years and 7.4% at 10 years.[12] In a 4-year follow-up of patients admitted for self-harm in the UK, the risk of dying by suicide was 30-fold higher than that of the general population.[13] These data point to the need of timely and effective interventions after a self-harm episode to reduce the risk of self-harm repetition and suicide.

Psychosocial interventions, such as psychotherapies or counselling interventions, are considered key therapeutic tools to prevent self-harm repetition.[14] Several studies investigated the efficacy of psychosocial interventions in adults with self-harm,[15–18] and pairwise meta-analyses (including a recent one from the Cochrane Collaboration[19]) of their findings having been published.[19 20] However, despite the fact different types of psychosocial interventions have shown some evidence of being effective in reducing self-harm repetition,[16] only few of them (eg, cognitive behavioural therapy (CBT)) are supported by a sufficient (ie, >3) number of randomised controlled trials (RCTs).[19] Additionally, little is known about whether a form of psychosocial intervention (eg, dialectical behavioural therapy) is superior to another one (eg, CBT) in preventing self-harm repetition. This is an important clinical question because if a superior intervention exists, this should be prioritised to maximise preventive efforts. However, there is a shortage of head-to-head comparisons of psychosocial interventions for the prevention of self-harm repetition, likely because RCTs are costly and particularly challenging in this field, as recruitment is difficult due to the relatively low prevalence of self-harm. While a previous meta-analytic study concluded that effect sizes of psychosocial interventions for self-harm are similar across several types of interventions,[20] this study does not provide a direct, quantitative comparison of such interventions. Providing a comparison across different intervention is however important for a clinical and public health point of view, as this would allow to prioritise interventions supported by evidence of superiority. Network meta-analysis (NMA) is the state-of-the-art statistical approach to gain insight about the comparative efficacy and/or tolerability/acceptability of several interventions.[21] Furthermore, an important advantage of NMA is that multiple interventions are simultaneously compared using both direct and indirect sources of evidence into a single network (figure 1). This is critical because suicidal behaviours are rare events, and capitalise on all sources of evidence (ie, direct and indirect comparisons) allows to significantly increase statistical power.

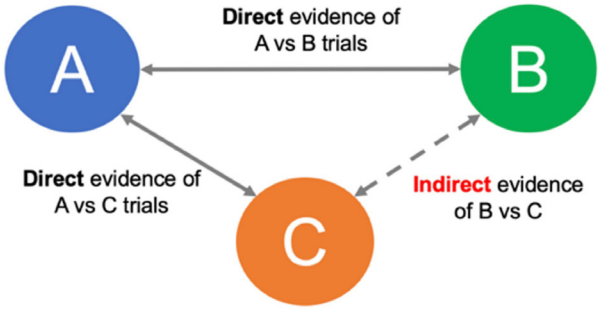

Figure 1 Direct and indirect evidence in network meta-analysis. Classic meta-analysis comparing two treatments (eg, treatment A vs treatment B) uses direct evidence from trials. This is known as pairwise meta-analysis. When the set of treatments differs across trials, this approach may greatly reduce the number of trials for each meta-analysis and makes it difficult to formally compare more than two treatments. This is addressed by network meta-analysis by using indirect evidence: direct evidence for treatment A versus B, and direct evidence for treatment A versus C allows one to compare treatment B and treatment C (indirect evidence).

METHODS

This study will be conducted between 1 September 2023 and 1 December 2024. This protocol has been developed following the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols[22 23] items, including the NMA extension.[24] Results will be reported following the same guidelines, and the complex intervention extension will be considered should the included study meet the criteria for being complex interventions.[25] Details of the methods are provided below, and inclusion/exclusion criteria are summarised in table 1.

Eligibility criteria

Types of studies to be included

We will include RCTs testing the efficacy of psychosocial interventions against a control condition (including another psychosocial intervention, drug therapy, treatment as usual or waiting list). We will include both open and blinded RCTs (which are the most commonly used designs for RCTs of non-pharmacological interventions, since the impossibility of performing double blinding), and no limitations will be applied for the length of the follow-up period, number of sessions and minimal number of participants. Additionally, we will include cluster-randomised trials but run a sensitivity analysis if we find substantial concerns regarding its inclusion (eg, bias due to broken allocation concealment, or missing intracluster correlation coefficients). We will exclude quasi-randomised studies and studies comparing different intensities or versions of the same intervention without a comparison group. For cross-over trials, we will consider only the first phase of the study (when data are available), as a 'carry over effect' cannot be excluded.

Table 1 Summary of the inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Study		
Study type	Randomised controlled trial (open and blinded; only first phase of a cross-over trials), cluster-randomised trials (with a sensitivity analyses)	Observational studies, quasi-randomised studies, studies comparing different intensities or versions of the same intervention
Length of follow-up	Any	No restriction
Publication year	Any	No restriction
Sample size	Any	No restriction
Country	Any	No restriction
Participants		
Age of participants	Adults (mean age ≥18 years)	Children and adolescents (mean age <18 years)
History of self-harm	Self-harm in the 6 months before the start of the trial	No self-harm, suicidal ideation only or self-harm more than 6 months before the start of the trial
Intervention		
Intervention	Psychosocial (eg, not uniquely pharmacological) interventions	Uniquely pharmacological interventions
Comparator	Any intervention or no intervention	No restriction
Length of the intervention (number of sessions)	Any	No restriction
Delivered by	Healthcare professionals	Lay persons (eg, 'buddy' programmes)
Setting	All (eg, inpatient, outpatient)	No restriction
Outcomes	Self-harm, suicide mortality, suicidal ideation, depression	Other outcomes

Participants

Adult participants (mean age: ≥18 years; both sexes) were included in RCTs testing the efficacy of a psychosocial intervention for the prevention of self-harm repetition. We will focus only on adults (and not children and adolescent) because self-harm behaviours in these populations have different psychopathological characteristics, and focusing on both populations may results in excessive heterogeneity. We will consider trials where the majority of participants reported at least one episode of self-harm in the previous 6 months.[19] Studies will be included irrespectively of the setting from which participants came (eg, inpatient or outpatient) as well as of their country of origin (eg, high-income, low-income and middle-income countries, as defined by The World Bank[26]).

Interventions

We will consider a broad range of psychosocial interventions, defined as non-pharmacological interventions provided by a trained professional that primarily uses forms of communication and interaction to assess, diagnose and treat dysfunctional emotional reactions, ways of thinking and behaviour patterns (American Psychological Association Dictionary of Psychology, https://dictionary.apa.org/psychotherapy). For instance, we will include both well-structured psychotherapies such as CBT as well as less structured, one-off interventions such as single-session problem-solving interventions or remote contact interventions (eg, based on postcards). Interventions will be categorised according to their similarities and theoretical approach. Based on previous meta-analyses and the specific literature on psychosocial intervention for self-harm,[19 27] we planned to categorise the interventions as described in table 2. Eligibility of any other possible forms of intervention will be discussed on a case-by-case basis by the team to establish if they meet the above definition. The categorisation of the studies will be defined via consensus within the review team (who have considerable experience in both research and clinical practice related to self-harm), after study selection is completed but before carrying out statistical analysis. Interventions using different delivery modalities of the same type of intervention (eg, face-to-face or telephone), or different intervention formats (eg, group or individual), will be categorised in the same categories, since current evidence does not clearly indicate substantial differences in intervention efficacy based on delivery modality or format.[28–33] However, if possible and feasible (eg, sufficient number of available studies), sensitivity analyses separating interventions by delivery modality and/or format will be conducted to allow future research to have a stronger evidence base to decide on the pertinence of subcategorising intervention based on these criteria.

Comparators

There will be no restrictions on the type of control. Categorisation of the comparators will be based on consensus discussions among members of the review team. From previous reviews[19] we expect the following comparators: treatment as usual (TAU); enhanced TAU (ETAU); and no intervention/waiting list. Although it may vary greatly across studies, TAU is defined as routine clinical care that the person would receive had they not been included in the trial, while ETAU is defined as TAU in some way, been supplemented by interventions that such as psychoeducation, assertive outreach or more regular contact with case managers (table 2). Patients receiving no intervention,

Table 2 Categorisation of psychosocial interventions

Categories	Definition
CBT	CBT helps people identify and critically evaluate the ways in which they interpret and evaluate events, and the impact of dysfunctional thoughts on behaviours and emotions. People learn strategies to help them change the way in which they think so that they can modify interpretations of emotions and events, as well as modify their behaviour. Learning problem-solving strategies is often part of CBT. CBT integrates concepts such as cognitive biases, cognitive restructuring and schemas.
Problem-solving therapy	Problem-solving therapy can be delivered as a stand-alone psychological intervention to help the person to learn skills to actively, constructively and effectively solve the problems that the person is facing in their daily life. It includes the following elements: definition of personal problems, generation of multiple solutions to each problem, selection of the best solution, the working out of a systematic plan for this solution, and evaluation as to whether the solution has resolved the problem.
Third wave therapies	Third wave therapies encompass therapies such as acceptance and commitment therapy and mindfulness-based therapies, which prioritise holistic psychological and behavioural processes associated with mental health. The focus is on opening clients towards their own experience, increasing self-awareness and promoting self-acceptance. Concepts such as metacognition, compassion, mindfulness, personal values and spirituality are frequently incorporated into what might otherwise be considered traditional CBT interventions.
DBT	DBT provides skills to regulate emotions, while promoting non-judgmental acceptance of painful and distressing thoughts and emotions (using mindfulness and acceptance strategies), as well as interpersonal effectiveness (using CBT-like, problem-oriented techniques).
Psychodynamic therapy	Psychodynamic therapy aims at enhancing the patient's understanding, awareness and insight about unconscious conflicts. The therapy often focuses in on developing insight about how the person's childhood experiences, past unresolved conflicts and historical relationships significantly affect the person's present life situation. The therapists also explore a person's dreams, fantasies and affects emerging within the therapeutic relationship (transference/countertransference).
Mentalisation-based therapy	Mentalisation-based therapy is a form of psychodynamic therapy that focuses on the person's ability to understand the behaviour of both one's self and others in terms of motivational and emotional states (intentional mental states). The aim is not developing insight, but the recovery of mentalising capacity via the attachment relationship with the therapist.
Non-directive supportive counselling and information	Usually refers to non-structured approaches providing information, empathic/active listening, supportive intervention and counselling.
Case management	Case management is a mean of coordinating services around the need of the individual. The person is assigned a 'case manager' who is expected to assess that person's needs, develop a care plan, arrange for care to be provided, monitor the implementation of the care plan and maintain contact with the person. We included studies in which case management was provided by the general practitioner.
Passive remote contact interventions	Low-intensity, low-resource and non-intrusive interventions that seek to maintain some contact with people by sending letters, brief text messages and postcards. These interventions provide a sense of ongoing concern, may mitigate the sense of social isolation, may help to improve knowledge about triggers and warning signs, provide information including on accessing help. Sometimes, these interventions are combined with emergency card interventions, which aim to enhance access to care by encouraging people to seek help when they feel distressed and facilitating access to on-demand emergency contact with health services.
Active remote contact interventions	Low-intensity, low-resource interventions that seek to maintain long-term contact with people by phone or other means and that include a healthcare professional talking with the person. Differently from the 'passive remote contact interventions', the healthcare professional is able to have a more active role.
Mixed interventions with psychotherapy elements*	A combination of multiple interventions into a multimodal approach that includes some form of structured psychotherapy, such as elements of behaviour therapy, thoughts recognition, problem solving or psychodynamic-oriented sessions.
Mixed interventions without psychotherapy	A combination of multiple interventions into a multimodal approach that does not have elements of psychotherapy or problem solving, such as combination of emergency department intervention followed by phone calls each month or by postcards.
Brief emergency department-based interventions	Interventions delivered in one session at the moment of admission or discharge from the emergency department. These interventions may include psychoeducation, information sheets, or more elaborated sheets to foster reflection on alternative behaviours in case of subsequent suicidal ideation.

Continued

Table 2 Continued

Categories	Definition
Safety planning-type intervention	Brief interventions that aim to reduce the imminent risk of self-harm by constructing a predetermined set of coping strategies and sources of support (eg, identification of warning signs, list of coping strategies, list of people to call to obtain support, removing means of suicide from the environment, list of personal reasons for living) in a written plan that can guides someone when they are experiencing suicidal thoughts, to help them avoid a state of intense suicidal crisis.
TAU	Defined as the routine clinical care that the person would receive had they not been included in the trial.
ETAU	TAU that has, in some way, been supplemented by interventions that may include providing psychoeducation, assertive outreach or more regular contact with case managers, and standard assessment approaches.
No intervention	Receiving no intervention, including staying on the waiting list for an intervention.

*If possible and relevant, different categories for different types of psychotherapy will be used, such as 'Mixed interventions with problem solving' or 'Mixed interventions with CBT'.
CBT, cognitive behavioural therapy; DBT, dialectical behavioural therapy; ETAU, enhanced TAU; TAU, treatment as usual.

including those on the waiting list for an intervention, will be considered in the no intervention/waiting list group.

Outcomes

The primary *efficacy outcome* will be the presence of self-harm, defined as any type of self-injurious behaviour, including self-poisoning, thus including suicide attempt (a potentially self-injurious behaviour associated with at least some intent to die) and non-suicidal self-injury (a self-injurious behaviour in which the intent to die is not present) at the time of the primary endpoint specified in the trial.[5] If data allow, different networks will be estimated based on the timing at end-point assessment (eg, short-term and medium/long-term end-points). Secondary outcomes will be: (1) suicide mortality, defined as death by suicide,[5] (2) suicidal ideation, defined as thoughts about taking action to end one's life[5] and (3) depression severity, defined as assessment of depressive symptoms with validated instruments (self-reported or assessed by others such as a clinician). We will consider analysing suicide attempt and non-suicidal self-injury separately (ie, distinguishing these outcomes based on the intentionality of the act, instead of considering both as self-harm), if sufficient data are available. The primary *acceptability outcome* will be retention in treatment, defined as the proportion of participants who completed the primary treatment protocol at the time of the primary endpoint specified in the trial. We expect that this endpoint will be pertinent only for interventions requiring multiple sessions, but not in one-off interventions. Potentially adverse events will also be documented and analysed as a secondary endpoint, if sufficient data are available.

Patient involvement

Patients and members of the public were not involved in the design of the study, but they will be involved in the interpretation of the results, definition of the implications of the findings, reporting and dissemination of our research.

Information sources

Data sources and search strategy

The most recent Cochrane systematic review on this topic[19] summarised evidence on the efficacy of psychosocial interventions for self-harm in adults published up to 1 July 2020. Our search strategy will rely on the one published in the Cochrane review. A health sciences librarian will update the search strategy so that the studies retrieved in the Cochrane review and the newly published evidence will be included in the present study. The searches will be performed in MEDLINE (Ovid), Embase (Ovid), PsycInfo (Ovid), CINAHL (EBSCO), Cochrane Central (Wiley), Cochrane Protocols (Wiley), LILACS and PSYNDEX from 1 July 2020 (Cochrane review last search date) to 1 September 2023. Full details on the search strategy can be found in this data repository: https://doi.org/10.5683/SP3/OPTNMD. The reference lists of identified trials will be screened to identify trials that potentially eluded our search. Finally, proceedings of recent (2020–2023) conferences organised by the largest scientific committees in the field (eg, International Association for Suicide Prevention (IASP), and Joint International Academy of Suicide Research (IASR) and American Foundation for Suicide Prevention International Summits on Suicide Research) will be searched. Finally, we will contact experts in the field via the IASP and IASR to potentially identify unpublished studies.

Selection process

Two reviewers will independently screen all the retrieved articles by title/abstract using Rayyan.[34] The full text of the selected articles will be then screened by two authors against the eligibility criteria for the inclusion in the study. Reasons for exclusion will be reported.

Data collection process

Data will be independently extracted by two authors using a predefined template including information on the study: authors, years, country, setting; participants:

sample size, age, sex and/or gender distribution, ethnicity distribution, type of diagnosis, presence/absence of pharmacotherapy coadministration and per cent of participants treated with medication; intervention and control condition: type of intervention (eg, CBT)/control condition (eg, TAU), format (eg, group therapy), delivery mode (eg, on-line), number of sessions, number of participants completing the trial; outcome: endpoint time, investigated outcomes; quantitative data: numbers (nominator and denominator) of participants reporting the binary outcomes at the endpoint; mean, SD and sample size at the endpoints for quantitative outcomes. All disagreements in study selection and data extraction will be resolved by a third author.

Risk of bias assessment

Two reviewers will independently assess risk of bias using the tool Risk of Bias 2 (RoB-2) tool,[35] which assesses five domains (bias arising from the randomisation process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, bias in selection of the reported result) as well as an overall bias evaluation. Each item within the five domains is assessed according to the risk of bias being low, high or other (not applicable/no information provided). All studies will be included in the quantitative analysis, but sensitivity analyses excluding studies with high risk of bias will be conducted.

Data synthesis

Pairwise meta-analysis

For each outcome, we will perform a direct comparison of the interventions using pairwise meta-analyses with a random-effect model. We will use (1) Self-harm Odds Ratio (with 95% CIs) as measure of effect for both efficacy and acceptability primary outcomes. OR will also be used as a measure of effect for the secondary outcome suicide mortality. Our rationale for using OR as a primary measure of effect size is based on potential bias of using risk ratio in random-effect meta-analyses, as described and empirically documented by Bakbergenuly *et al*.[36] Since suicidal ideation and depression severity are usually measured on a continuous scale, standardised mean difference will be used as a measure of effect. These measures of effects will be computed from the raw data (eg, numbers and means). If different scales are used for the same outcomes across studies, we will convert effect size across studies to the chosen common effect size using standard conversion rules.

Network meta-analysis

To assess the comparative efficacy of all treatment comparisons, including direct and indirect comparisons, we will perform for each outcome an NMA with a random-effect model in a frequentist framework. We will account for correlations induced by multiarm studies. Ranked forest plots will be used to represent graphically the results of the NMA, in which all comparisons with the same comparator will be plotted, and conclusions from an NMA in terms of recommendable, less recommendable and not recommendable treatments will be drawn using a minimally contextualised framework as described in Brignardello-Petersen *et al*.[37]. Additionally, we will also provide a ranking of the interventions based on the Surface Under the Cumulative Ranking Curve (SUCRA) as secondary analysis. We will use ranked forest plot as primary analysis because they provide a visual representation of the relative efficacy of the interventions as well as the precision of the estimates, which are both clinically important elements that are not distinguished using the ranking based on SUCRA. Finally, Vitruvian plot will be used to graphically present absolute estimates and relative performance of competing interventions against a common comparator for several outcomes of interest.[38]

Assessment of transitivity and inconsistency

We will first examine if potential effect modifiers are not differentially distributed across comparisons. We will do this by summarising means for each subgroup by key effect modifiers such as psychiatric diagnoses of patients, intervention format, intervention intensity and time at outcome assessment. When we find the network to be highly intransitive, we will synthesise the evidence only narratively. We will then assess consistency of the network statistically by (1) global test of inconsistency and (ii) local tests of inconsistency.

Assessment of heterogeneity

In pairwise meta-analysis, heterogeneity will be assessed using the τ^2 and I^2 (measuring for the proportion of observed variance that reflects real differences in effect size). In NMA, statistical heterogeneity will be assessed based on the magnitude of the heterogeneity variance parameter (τ^2) estimated from the NMA models. We will compare the magnitude of the heterogeneity variance with the empirical distribution as derived by Turner *et al*.[39] We will also estimate a total I^2 value for heterogeneity in the network as described by Jackson *et al*.[40] Significant heterogeneity would suggest that the transitivity assumption (ie, absence of systematic differences between comparisons other than across interventions, so that participants may hypothetically have been randomised in any compared interventions) is unmet. In case we found significant heterogeneity or inconsistency, and that sufficient studies are available, we will use meta-regression and subgroup analyses to explore the sources of heterogeneity. We will test the following effect modifiers, if data are available: (1) publication year; (2) psychiatric diagnosis of participants; (3) setting (eg, inpatient/outpatient); (4) intervention intensity; (5) risk of bias; (6) sample size; (7) sex and/or gender; (8) age; (9) time at outcome assessment; (10) intervention format (eg, group/individual, if not possible considering them separately); (11) delivery mode (eg, online/in-person, if not possible considering them separately); (12) country of origin; and (13) ethnicity.

Assessment of publication bias

We will assess publication bias by visually inspecting the contour-enhanced funnel plot, whatever the number of trials, and run the statistical test for funnel plot asymmetry if there are more than 10 studies involved.

Credibility of the evidence

Two reviewers will independently assess the credibility of the evidence using the Confidence in NMA (CINeMA) tool. CINeMA allows the evaluation of the credibility of available evidence according to six domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. All disagreements will be resolved by a third author. As per the RoB-2 rules, we will use the average RoB per comparison to rate the within-study bias for each mixed or indirect estimate, we will use OR=0.8 (or 1.25) as the threshold to examine imprecision and heterogeneity, and we expect indirectness to be qualitatively judged as per the nature of the included studies.

ETHICS AND DISSEMINATION

Ethics

As this is the protocol of an aggregate-data level NMA, no ethical approval was obtained.

Dissemination

The results of this study will be disseminated nationally and internationally, via conferences, publications in peer-reviewed journals in the field of psychiatry and psychology, and events organised by people with lived experiences.

DISCUSSION

This study will provide evidence on the efficacy and acceptability of psychosocial interventions for the prevention of self-harm in adults by performing, to our knowledge for the first time, a NMA. A key strength of this study is the use a state-of-the-art approach to combine evidence using both direct and indirect comparisons of interventions. Given the shortage of head-to-head RCTs, the use of NMAs can maximise information available through existing trials. Furthermore, our study will provide a ranking of interventions that will be useful in clinical decision-making. Limitations of our study will depend on meeting the assumption of the NMA methodology. In particular, heterogeneity (ie, variability within direct and indirect comparisons due to clinical and methodological reasons), inconsistency (ie, discrepancy between direct and indirect comparisons) and bias may influence effect estimates obtained from NMA. To alleviate this limitation, we will apply the aforementioned methods to assess, quantify and deal with heterogeneity, inconsistency and bias. Furthermore, given the heterogeneity of psychosocial interventions and the relatively small number of expected RCTs, our categorisation of psychosocial interventions was mainly based on the theoretical approach. However, current frameworks for the categorisation of healthcare interventions emphasise the need to consider other aspects, including the intensity and the provider of the intervention.[41] We expect that the available evidence will not allow us to take these important aspects into account, therefore the implication of this limitation will be discussed in the manuscript reporting our findings. Finally, although categorisation of psychosocial interventions was based on consensus among experienced clinicians, some intervention may be heterogeneous and meet multiple criteria. This aspect will be acknowledged and discussed in our article.

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Acknowledgements MO holds a FRQ-Santé Chercheur-Boursier Junior one award. M-CG holds a Canada Research Chair Tier two from the Canadian Institutes of Health Research. GT holds a Canada Resarci Chair Tier one from the Canadian Institutes of Health Research. AC is supported by the National Institute for Health Research (NIHR) Oxford Cognitive Health Clinical Research Facility, by an NIHR Research Professorship (grant RP-2017-08-ST2-006), by the NIHR Oxford and Thames Valley Applied Research Collaboration and by the NIHR Oxford Health Biomedical Research Centre (grant NIHR203316). The views expressed are those of the authors and not necessarily those of the UK National Health Service, the NIHR, or the UK Department of Health. SC is supported by the following grants: 101095568-HORIZON- HLTH-2022-DISEASE-07-03 (European Research Agency) and NIHR203684, NIHR203035, NIHR130077, NIHR128472, RP-PG-0618-20003 (National Institute for Health and Care Research)

Contributors MO, AJG, DO, JB, AC, TAF, DS, CDG, AI, GT, M-CG and SC contributed to the planning, conception and design of the protocol of this study. JB led to the design of the planned search strategy. MO drafted the first version of the paper and acquired funding. MO, AJG, DO, JB, AC, TAF, DS, CDG, AI, GT, M-CG and SC contributed to important intellectual content and to the reporting of the work in this paper.

Funding This work was supported by a grant from the Fonds de Recherche du Québec (FRQ) Santé via le Réseau Québecois sur le Suicide, les Troubles de l'Humeur et les Troubles Associés (grant #268065) awarded to MO and FRQS Société et Culture Research Team Support Programme awarded to MCG). Funders have no role in data collection, analysis, interpretation and decision to publish the article.

Competing interests AC has received research, educational and consultancy fees from INCiPiT (Italian Network for Paediatric Trials), CARIPLO Foundation, Lundbeck and Angelini Pharma. TAF reports personal fees from Boehringer-Ingelheim, DT Axis, Kyoto University Original, Shionogi and SONY, and a grant from Shionogi, outside the submitted work. In addition, TAF has patents 2020-548587 and 2022-082495 pending, and intellectual properties for Kokoro-app licensed to Mitsubishi-Tanabe. SC declares honoraria and reimbursement for travel and accommodation expenses for lectures from the following non-profit associations: Association for Child and Adolescent Central Health (ACAMH), Canadian ADHD Alliance Resource (CADDRA), and British Association of Pharmacology (BAP) for educational activity on ADHD. The other authors declare no competing interests.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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