



Synopsis

Reducing self-harm in adolescents: the RISA-IPD comprehensive synopsis

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Abstract

Background: Self-harm is common in adolescents and a major public health concern. Evidence for effective interventions is lacking. An individual participant data meta-analysis has potential to provide more reliable estimates of the effects of therapeutic interventions than conventional meta-analyses and to explore which treatments are best suited to certain groups.

Methods: A systematic review and individual participant data meta-analysis of randomised controlled trials of therapeutic interventions to reduce repeat self-harm in adolescents with a history of self-harm and who had presented to clinical services. We searched Cochrane Library, EMBASE, trial registers and other databases for randomised controlled trials published in January 2022. Eligible randomised controlled trials compared any therapeutic intervention against a control, aimed to reduce self-harm in adolescents (11–18 years old), with past self-harm presenting to clinical services, and collected outcome data on self-harm or suicide attempts.

Interventions reviewed were grouped into nine categories: cognitive-behavioural therapy; dialectical behaviour therapy; family therapy; group therapy; mentalisation based, psychodynamic, cognitive analytic therapy; multisystemic therapy; problem-solving, psychoeducation, support; postcards, tokens, documents (postcards/tokens); and other single session, brief interventions. Control interventions were all either treatment as usual or enhanced treatment as usual and were not usually well described. There were no 'no treatment' controls except in the postcard/document/token studies.

Primary outcome was repetition of self-harm at 12 months. Other outcomes included repetition of self-harm at other time points, overall mental health, depressive symptoms, thoughts of suicide, quality of life and death.

Two-stage random-effects individual participant data meta-analyses were conducted overall and by intervention, and to examine interaction between treatment received and participant characteristics. Secondary analyses incorporated aggregate data from randomised controlled trials without individual participant data. Metaregression explored moderating study effects.

Results: We identified 39 eligible studies, from 10 countries, where we sought individual participant data (18 studies with full sample eligibility, 21 with partial sample eligibility). We obtained individual participant data from 26 studies of 3448 eligible participants. We used published data from a further seven studies where individual participant data were not available for a combined individual participant data aggregate data meta-analysis (698 participants).

For our primary outcome, repetition of self-harm, only six studies were rated as low risk of bias.

There was no evidence that intervention/s were more or less effective than controls at preventing repeat self-harm by 12 months using individual participant data (odds ratios 1.06, 95% confidence interval 0.86 to 1.31) or individual participant data + aggregate data (odds ratios 1.02, 95% confidence interval 0.82 to 1.27) and no evidence of heterogeneity of treatment effects on study and treatment factors. We found no evidence that intervention was more or less effective than control for secondary outcomes, except general psychopathology and suicidal ideation at 12 and 6 months, respectively.

Across all interventions, participants with multiple prior self-harm episodes showed evidence of improved treatment effect on self-harm repetition 6–12 months after randomisation [odds ratios 0.33 (95% confidence interval 0.12 to 0.94), studies = 9, $n = 1771$]. Modest evidence suggesting differential treatment effects based on participants' age, gender, self-harm method, and anxiety levels are noted.

Limitations: A significant limitation was missing individual participant data where authors were unable to share data; we offset this by including published data in secondary individual participant data plus aggregate meta-analysis. A wide range of interventions were evaluated and lacked replication.

There was variability in the definitions and timings of outcomes, measures used for data collection, and available moderator data, with little consistency across studies.

Conclusions: More attention needs to be paid to seeking appropriate consent from study participants for data-sharing. We found no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control for reducing repeat self-harm. We are therefore unable to recommend any specific intervention to prevent repetition of self-harm in adolescents.

We observed evidence and trends indicating more effective interventions within specific subgroups. Analysis was constrained due to scarcity of data concerning common baseline characteristics, outcomes, and follow-up lengths. We recommend efficient, adaptive platform trial designs to tackle research questions and ascertain the most effective interventions for different groups, covering available treatments.

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A plain language summary of this synopsis is available on the NIHR Journals Library Website <https://doi.org/10.3310/KKBB1164>.

Background

Some text in this synopsis has been reproduced from Wright-Hughes *et al.*¹ and from Wright-Hughes *et al.*² These are Open Access articles distributed in accordance with the terms of the Creative Commons Attribution (CC BY 4.0) license, which permits others to distribute, remix, adapt and build upon this work, for commercial use, provided the original work is properly cited. See: <https://creativecommons.org/licenses/by/4.0/>. The text below includes minor additions and formatting changes to the original text.

Self-harm is defined by the National Institute for Health and Care Excellence as any form of non-fatal self-poisoning or self-injury (including cutting, taking excess medication, attempted hanging, self-strangulation, jumping from height, running into traffic), regardless of suicidal intent.³ This includes definitions of non-suicidal self-injury (NSSI) commonly used by US researchers and suicidal behaviour, where lack of intent is assumed by reference to the method of self-harm.

Self-harm is common in young people. A meta-analysis of 172 community-based studies of adolescents from 1990 to 2015 reported a lifetime prevalence of 16.9%, with rates increasing over time.⁴ Self-harm also has serious consequences. Repetition of self-harm is common, occurring in 27.3% of the sample in the Multicentre Study of Self Harm in England.⁵ The risk of death by suicide following earlier self-harm is increased.⁶ Suicide is the second commonest form of death in those aged 10–24 years old.⁷

It is therefore not surprising that self-harm is a matter of major public health concern in the UK.⁸ Effective interventions that reduce the likelihood of self-harm repetition are badly needed, to reduce distress in young people and their peers and families, to save lives, and to reduce the burden of cost on health and social care services. Unfortunately, such interventions have not yet been identified. The most recent Cochrane review in 2021⁹ found 'only uncertain evidence regarding a number of psychosocial interventions in children and adolescents who engage in SH'. Other analyses came to similar conclusions.^{10–12} The Cochrane review suggested

further evaluation of dialectical behaviour therapy for adolescents (DBT-A),⁹ and the National Institute for Health and Care Excellence (NICE) guideline¹² recommended 'consideration' of DBT-A for children and young people but otherwise made no firm recommendations.

Participant-, treatment-, and study-level factors may all influence intervention effectiveness and outcomes. Clinicians and young people report that self-harm occurs for many different reasons. Treatment trials to date have applied a single treatment to groups of young people who are likely to have self-harmed for very different reasons. It seems reasonable to hypothesise that there may be subgroups of young people within the self-harming population who will respond differently to different interventions. The purpose of this study was to explore this hypothesis.

We chose to conduct an individual participant data (IPD) meta-analysis as this provides more robust estimates of the effects of therapeutic interventions for self-harm than conventional meta-analyses that rely on aggregated information and reported analyses.¹³ IPD meta-analyses also increase the power to detect interaction between treatment and clinical and sociodemographic characteristics, and to explore moderating effects.

This paper summarises the methods and results of an IPD meta-analysis [incorporating aggregate data (AD) meta-analysis where IPD were not available] of randomised controlled trials (RCTs) of interventions to prevent repetition of self-harm in young people.

We summarise the methods and results of a systematic search to identify eligible studies, our assessment of bias in the studies identified, the pooled treatment effects, and the study, treatment and participant level moderating effects.

Methods

This project was carried out following a successful bid for a commissioned call from NIHR, which specified the need to conduct an IPD meta-analysis. The project was registered with PROSPERO (CRD42019152119),¹⁴ a protocol has been published,¹ and the project is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-IPD guidelines.¹⁵

Analyses were conducted according to a pre-specified statistical analysis plan (SAP) (see [Report Supplementary Material 1](#)).

Objectives

The objectives were to:

- conduct a systematic literature search and systematic study selection to identify relevant research teams and studies
- invite identified research teams to contribute data to enable us to form a collaborative group and conduct IPD meta-analysis
- conduct IPD meta-analysis to:
 - provide updated estimates of the pooled treatment effect of therapeutic interventions for self-harm compared with any non-active control.
 - identify subgroups of adolescents based on participant-level covariates, in whom therapeutic interventions are more effective.
 - explore moderating study and intervention effects.
 - provide clearly defined research recommendations for future clinical practice and RCTs.

Study design

Systematic review and IPD meta-analysis of therapeutic interventions to reduce self-harm in adolescents with a history of self-harm who had consequently presented to clinical services. Where IPD are not available, AD will be incorporated in secondary meta-analyses.

Eligibility criteria

Participants

The participants' eligibility criteria included:

- all adolescents of any gender or ethnicity aged 11–18 years, where 18 is defined as up to the 19th birthday at the point of randomisation.
- who have self-harmed at least once at any time prior to randomisation.
- presented to clinical services for self-harm, where self-harm includes suicide attempt and NSSI and excludes suicidal ideation without explicit self-harm.

No restrictions were placed on whether participants in the studies we included had comorbid mental or physical health conditions or intellectual disability. However, nearly all the studies we included in our analysis excluded young people with concurrent psychotic disorder or moderate to severe learning difficulties.

Self-harm was defined as any form of non-fatal self-poisoning or self-injury (including cutting, taking excess medication, attempted hanging, self-strangulation, jumping from height, running into traffic), regardless of suicidal intent.³ Self-harm could be self-reported.

Interventions

Any intervention, delivered by care provider(s), with an aim to reduce subsequent self-harm, including psychological or pharmacological interventions. Prevention-based interventions not targeted specifically at adolescents who have presented to clinical services with self-harm and intensive inpatient-based interventions were excluded.

Therapeutic interventions were grouped by consensus (DC, DO, PF), according to study published descriptions, theoretical underpinnings, supplementary material and manuals. The categories were: cognitive-behavioural therapy (CBT); dialectical behaviour therapy (DBT); family therapy (FT); group therapy (GT); mentalisation based, psychodynamic, cognitive analytic therapy (MBT/CAT); multisystemic therapy (MST); problem-solving, psychoeducation, support (PST); postcards, tokens, documents (postcards/tokens); other single session, brief interventions.

Controls

Any inactive or any active control.

Primary outcome

Repetition of self-harm: defined as a cumulative binary outcome from randomisation to last available follow-up period within 3, 6, 12, 18 and 24 months post randomisation.

The primary time period was 12 months post randomisation. For the primary outcome, this included studies where the follow-up assessment of self-harm took place between > 6 and ≤ 12 months post randomisation, with self-harm measured from randomisation.

Secondary outcome

- Time to repetition of self-harm.
- Pattern of self-harm repetition (any self-harm within 6-month periods post randomisation: 6–12 months, 12–18 months, 18–24 months).
- General psychopathology: score on a self-report measure of emotional and behavioural problems.
- Depression: score on a self-report measure of depression.
- Suicidal ideation: score on a self-report measure of suicidal ideation.
- Quality of life: score on a self-report quality-of-life scale.
- Death of adolescent.

Follow-up assessments were grouped in the short term (up to 3 months post randomisation), and at 6, 12, 18 and 24 months post randomisation. Where studies included

assessments beyond 24 months, data were included where feasible and grouped as ≥ 24 months post randomisation.

Setting/context

All countries of origin, any method of referral but ongoing intervention delivered in outpatient or community (school and voluntary sector) settings. We excluded intensive inpatient-based interventions as these were unlikely to be applicable to UK settings.

Studies

All RCTs, from the first available study, with any randomised design, length of follow-up and quality, in which data, aligning with our primary outcome, relating to self-harm or suicide attempts had been collected.

We included studies in which only a subset of participants met our eligibility criteria. Studies with < 20 eligible participants were excluded to ensure the logistical effort in obtaining, cleaning and organising the data was commensurate with the contribution of the data set to the analysis.

Identifying studies

We undertook a scoping exercise prior to project commencement (in 2018) to determine the potential for eligible RCTs to be identified by harvesting studies included in published systematic reviews. The systematic reviews search identified five reviews that included 22 RCTs meeting our criteria.^{16–20} Our assessment of these reviews indicated eligible studies may have been missed if they were unpublished, recently published or contained $< 85\%$ adolescents as participants. To ensure greater coverage of eligible RCTs, while minimising the number of records needing to be screened, we therefore used a two-stage approach.

This second step was important to find RCTs published since the date of searches in our included systematic reviews, or to compensate for insufficient search methods, for example, where ongoing trials registries had not been searched.

Search 1: Systematic reviews of eligible randomised controlled trials

In June 2019, we searched information resources for systematic reviews of interventions for self-harm in adolescents (*Table 1*). Searches were developed for the concepts: self-harm, adolescents, and systematic reviews. Subject headings and free text words were identified for use in the search concepts by the information specialist and project team members. Further terms were identified and tested from known relevant papers, and the strategy

was not limited by publication date or language. The search was peer-reviewed by an information specialist using the Peer Review of Electronic Search Strategies (PRESS) checklist.²¹ See [Appendix 1](#) for complete details of search strategy. The results of the database searches were stored and deduplicated in EndNote X9 [Clarivate Analytics (formerly Thomson Reuters), Philadelphia, PA, USA].

Eligible systematic reviews were selected, and potentially eligible RCTs were harvested from the references linked to their included studies. Where it was unclear which references had been included in a review, we obtained reference records for the entire bibliography. All references harvested from systematic reviews were deduplicated and stored in an EndNote library, before combining with references found in Search 2 for RCTs.

Search 2: Additional randomised controlled trials

The search methods of the included systematic reviews were scrutinised to determine what supplementary searches were necessary to ensure our attempts to find all eligible RCTs were comprehensive, up-to-date and mitigated publication bias. We then designed search strategies for the search concepts 'adolescents', 'self-harm or suicide' and RCTs, by incorporating search terms used in published reviews, identifying terms from known relevant studies, checking subject heading lists and from our project expert's suggestions. The Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)²² was used for the Ovid MEDLINE search. The PsycInfo® (American Psychological Association, Washington, DC, USA) and Cochrane Central Register of Controlled Trials (CENTRAL) searches were limited to studies published from 2015 as it is most likely that studies pre-2015 would have been identified and harvested from the Witt *et al.* review²³ and our other harvested reviews. The MEDLINE and EMBASE searches were limited to studies published in the last 12 months (2018–9). They covered the time-lag when RCTs are available in MEDLINE or EMBASE but have not yet been included in the Cochrane CENTRAL. The searches of all other databases and websites were not limited by date, and no searches were limited by publication language. Searches were peer-reviewed by another information specialist using the PRESS checklist.²¹ See [Appendix 2](#) for full search strategies.

The August 2019 search results were combined and deduplicated with the RCTs harvested from the systematic reviews from Search 1, in EndNote. Reference lists of

included studies and reviews were scrutinised for further relevant studies. The resultant set of records was imported into Covidence (Melbourne, VIC, Australia) to screen for eligible RCTs and their study contact from whom we could request IPD.

Updated searches

On 11 February 2021 and 21 January 2022, we ran further searches to identify relevant RCTs that had been published since our 2019 searches. New studies would be incorporated in the aggregate meta-analysis and not used to seek IPD, as we recognised there would not be time to request, access and include their IPD. For this reason, the update searches were only conducted in databases that contained published studies (see [Table 1](#)).

Update searches had minor changes compared to the 2019 search due to new indexing terms used by databases, and discovery of further relevant index terms. The MEDLINE and Cochrane CENTRAL updated searches included a new medical subject heading (MeSH) 'Suicide, Completed/'. The EMBASE search included a new Emtree term '*Opiate Overdose/' and previously missed term 'High School Student/'. Conference abstracts were excluded from the 2022 EMBASE search (but not 2019 or 2021), as the team was close to completing the review and would not have time to follow up trials mentioned at conferences. The PsycInfo search included previously missed headings 'head banging/', 'self-inflicted wounds/', 'self-poisoning/'. Headspace had an updated search strategy to search its research database rather than its webpage; however, the MHMRC search remained the same. The updated search strategies are listed in [Appendix 1](#) and [Appendix 2](#).

Reference lists of included studies and reviews were scrutinised for further relevant studies, and collaborative group members asked if they knew of other studies, but none were forthcoming.

The results of the update searches were stored in EndNote, duplicate records were removed, and only previously unseen records were included in the Covidence review for screening.

Selecting studies

All titles and abstracts were initially reviewed independently by two reviewers (DC and AW-H) within Covidence. The full text of any potentially eligible record was then examined independently by the same reviewers. Disagreements in screening decisions were discussed by reviewers and, if agreement could not be reached, adjudicated by a further reviewer (RW). We initially included protocols in the title/abstract screening and any

TABLE 1 Information resources searched

Search	Academic databases	Websites and other grey literature sources
Search 1 Systematic reviews of interventions for self-harm in adolescents	Cochrane Database of Systematic Reviews (Wiley) Issue 6 of 12, June 2019 EMBASE Classic + EMBASE (Ovid) 1947–20 June 2019 Epistemonikos https://epistemonikos.org/ Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946–20 June 2019 PsycInfo (Ovid) 1806–Week 2, June 2019	PROSPERO https://crd.york.ac.uk/prospero/
Search 2 Additional RCTs of interventions for self-harm in adolescents	Cochrane Central Register of Controlled Trials (Wiley) Issue 8 of 12, August 2019 EMBASE Classic + EMBASE (Ovid) 1947–19 August 2019 Epistemonikos https://epistemonikos.org/ Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946–19 August 2019 PsycInfo (Ovid) 1806–Week 1, August 2019	ClinicalTrials.gov https://clinicaltrials.gov/ Conference Proceedings Citation Index–Science (Web of Science) 1990+ Conference Proceedings Citation Index–Social Science and Humanities (Web of Science) 1990+ Dissertations and Theses A&I (ProQuest) Europe PMC Grantfinder https://europepmc.org/grantfinder International Clinical Trials Registry Platform https://apps.who.int/trialsearch/ Headspace National Youth Mental Health Foundation https://headspace.org.au/ National Health and Medical Research Council (Australia) https://nhmrc.gov.au/
Update of Search 2 on 11 February 2021 and again on 21 January 2022	Cochrane Central Register of Controlled Trials (Wiley) Issue 1 of 12, January 2022 EMBASE Classic + EMBASE (Ovid) 1947–20 January 2022 Epistemonikos https://epistemonikos.org/ Ovid MEDLINE(R) ALL 1946–20 January 2022 APA PsycInfo (Ovid) 1806–Week 3, January 2022	Headspace National Youth Mental Health Foundation https://headspace.org.au/ National Health and Medical Research Council (Australia) https://nhmrc.gov.au/

other papers that were related to the main study paper to ensure a complete set of data as possible and to assist in finding study contact persons.

Where records were identified in any of the searches, but it was unclear from the study publication if they met our eligibility criteria, a clarification process was followed. Initially, additional study publications, published study protocols and/or trial registrations were sought. If this did not enable an eligibility decision to be made, direct contact was made with the study authors to seek further information. Strenuous efforts were made to establish contact, starting with e-mails to lead and corresponding authors. If this was not successful, we systematically sent e-mails to all other authors, conducted internet searches for authors who might have moved location, contacted heads of departments and used informal networks. Despite this, it was not always possible to achieve successful contact and clarification.

Data collection

Once agreed that a trial was eligible, authors were contacted via e-mail with an invitation letter and brief project summary asking for agreement in principle to (a)

share data and (b) join our Study Collaborative Group (see [Report Supplementary Material 2](#)). Some primary study authors informed us that data were no longer available. Most others had many queries about the practicalities and ethics of data-sharing. Authors with concerns were told that sharing of limited data sets would be possible if full sharing was not possible.

When willingness to share data was agreed in principle, a formal data-sharing agreement (DSA) was sent (see [Report Supplementary Material 3](#)). The DSA included a complete list of the data items requested: baseline participant demographics and clinical data, details of therapeutic intervention, and outcomes, prioritising the primary outcome. This was then signed on behalf of the data holder's institution and countersigned by the University of Leeds. On receipt of a signed DSA, primary study authors were asked to provide pseudonymised data sets in whatever format was convenient to them, alongside data dictionaries, original SAPs and relevant statistical programming code, where possible. Data were transferred securely via a Secure File Transfer service to the Clinical Trials Research Unit (CTRU) at the University of Leeds.

The raw data received were saved in a restricted folder on receipt, prior to any modification of the data. Data were read into SAS and translated into English, where required. All information collected during the study was kept strictly confidential. The CTRU complies with all aspects of the 2018 Data Protection Act, which incorporates the European Union General Data Protection Regulation. At the end of the study, original data sets provided by collaborating trialists will be destroyed and the study data set securely archived at the CTRU for a minimum of 5 years.

Where IPD were not available, but the entire study sample was eligible, AD [number of participants/events, mean, standard deviation (SD)] were extracted from study reports and publications, where possible, by AW-H and verified by DS. Where necessary, we contacted authors for further information, where outcomes were collected but suitable AD were not reported. No analysis was possible for studies where IPD were not shared but only a part of the sample was eligible, as it was not possible to disaggregate published data to identify the eligible participants. Study-level variables relating to study conduct and design, methodology and clinical factors were extracted from publications by AW-H (verified and categorised by DC).

Data items

Data items for collection (see [Report Supplementary Material 3](#)) were selected based on agreed definitions of self-harm and on the evidence of factors known to influence the likelihood of repetition of self-harm. This was supplemented by input from a patient and public involvement and engagement (PPIE) group of young people with lived experience of self-harm, who suggested items that they believed would be of relevance.

Data integrity

All IPD supplied were subjected to a range of checks. Published statistics were replicated, where possible, and data checked for missingness, excluded participants, consistency and outliers, balanced randomisation and follow-up across arms. Issues and discrepancies were raised and rectified directly with the study contact/s, where possible. After completion of checks, individual trial data sets were mapped to a master data set. Outcomes and baseline characteristic variables of interest were manipulated to ensure consistency across data sets.

Risk of bias in individual studies

We assessed risk of bias (RoB) using version 2 of the Cochrane RoB tool for randomised trials (RoB2).²⁴ Each study was rated by two assessors independently (DC and either FM, AT or ED). Assessors reviewed the primary trial

publication and relevant trial registrations and associated protocol and methods papers. A third assessor (AW-H) adjudicated on disagreements. Domain 3 of RoB2 relates to bias due to missing outcome data. For 10 eligible studies, we judged that outcome data within the study had been collected in meaningfully different ways with some data, usually the primary outcome, being collected from hospital or medical records and other data (usually secondary outcomes such as depression, suicidal ideation, etc.) being collected from questionnaires or researcher interviews.

In one example, the Self-Harm Intervention: Family Therapy study,²⁵ the primary outcome was obtained from routinely collected hospital data and was available for almost all (96%) of the large (832) sample. Secondary outcomes in this study were obtained from researcher interviews with participants and were only available for 40–60% of the sample. As these two data collection methods seemed to materially affect the amount of missing data, we therefore decided to complete two RoB2 assessments for these 10 studies, 1 for each method of data collection.

In line with PRISMA-IPD guidance, following receipt of IPD, further adjustments were made to RoB ratings, where information became available that was not in the published trial manuscripts.¹⁵

Synthesis methods

Planned analyses are reported in full in the SAP (see [Report Supplementary Material 1](#)).

Data were analysed using SAS 9.4 (Institute S. SAS/ACCESS 9.4 Interface to ADABAS: Reference. SAS Institute Cary NC; 2013) and STATA 17 (StataCorp. Statistical Software: Release 17. College Station, TX: StataCorp LLC; 2021). Analyses were based on intention to treat (ITT), including all participants as randomised, regardless of withdrawal or protocol compliance. Primary analyses were based on available data, conducted separately at each time period, overall and by therapeutic intervention.

Treatment effects are expressed as odds ratios (ORs), hazard ratios (HRs) and standardised mean differences (SMDs). Where outcomes comprised continuous data from different scales, IPD scores were standardised in each study and time period, using the mean and pooled SD with approximate *Hedges' g* adjustment.

Pooled treatment effects

We used a two-stage approach,²⁶ estimating pooled treatment effects in each study separately, then pooling aggregate results. Step 1 used logistic (with Firth's

penalized likelihood to account for rare events), linear and Cox proportional hazards regression, adjusted for age (continuous) and gender. Analyses accounted for cluster-randomisation, using multilevel mixed-effects regression with a random cluster effect. Step 2 used random-effects meta-analysis allowing for heterogeneity associated with different study characteristics. Estimation used REML,²⁷ and confidence intervals (CIs) were derived using the Hartung-Knapp-Sidik-Jonkman (HKSJ)²⁸ approach to allow for uncertainty in variance estimates. Heterogeneity in treatment effects was assessed using τ^2 (variability of the true effect size under a random-effects model) and I^2 (proportion of total variability due to between-study heterogeneity).

Study and treatment moderators

Random-effects subgroup analysis (categorical variables) and metaregression (continuous variables) were used to explore study-level sources of between-study heterogeneity on treatment effect estimates, and specifically the impact of (1) clinical diversity in participant populations, (2) intervention delivery and (3) methodological diversity of study conduct and design. We used two-stage IPD plus AD meta-analyses to maximise the number of studies included. Analysis was conducted separately for each moderator, across all interventions and on the primary outcome.

Candidate moderators were:

- full versus partial sample eligible
- pilot/feasibility versus effectiveness design
- study sample size powered versus not
- USA versus other (differences in self-harm definition)
- low RoB versus some concerns versus high
- self-report data/researcher interview versus hospital/medical records
- control treatment as usual (TAU)/standard care/assessment versus enhanced treatment as usual/good clinical care versus active
- group element to intervention
- family element to intervention
- low, medium, high intervention intensity
- years since primary publication
- number of eligible participants
- treatment duration
- number of planned treatment sessions.

Adolescent moderators

A two-stage random-effects process²⁶ was employed, first estimating the interaction between the treatment received and the characteristics of the participants in each study providing IPD separately, and then combining the

aggregate results. We used two-stage IPD meta-analyses only as appropriate AD were not available from studies not providing IPD. Analysis was restricted to 6- and 12-month time points, as they encompassed all studies with available outcomes.

Key moderators were pre-specified for investigation across all primary and secondary outcomes. Further additional moderators, pre-specified for the primary outcome, were examined if present in at least half of the trials and applied to secondary outcomes where effects were identified. Moderators identified post hoc from available IPD were incorporated into the analysis in the same manner as the additional moderators.

Key moderators were:

- age
- gender: male, female
- presenting self-harm method: self-injury, self-poisoning, combined
- depression: presence and severity
- borderline personality disorder (BPD).

Additional moderators were:

- previous self-harm episodes: ≤ 2 , multiple
- family dysfunction: presence and severity
- unemotional/callous traits
- anxiety disorder
- ethnicity: White, other
- LGBTQ status
- autistic spectrum disorder (ASD)
- history of abuse
- eating disorder.

Emerging moderators were:

- self-harm outcome/severity
- intellectual disability
- looked after children (out-of-home care)
- psychotropic medication
- physical health problem
- suicidal ideation: presence and severity.

Additional analyses

Confidence intervals without the HKSJ adjustment are also provided to support comparison to previous meta-analyses.

Secondary analyses of the pooled treatment effects incorporated available published AD²⁹ for studies where IPD were not available. To ensure consistency in treatment

effect estimates obtained from IPD and AD, step 1 analysis of IPD was not adjusted for age and gender.

Sensitivity analyses were conducted to test the robustness of our conclusions regarding pooled treatment effects to our analysis methods by imputing missing IPD using multiple imputation, undertaking one-stage IPD meta-analysis, and excluding studies of high RoB (for the primary outcome). Due to the limited differences in findings on the overall pooled treatment effects, and the complexity and volume of analyses conducted, these sensitivity analyses were not repeated for moderator analyses.

Risk of bias across studies

Pairs of authors (DC, FM, AT, ED) independently assessed the quality of included studies using version 2 of the Cochrane RoB tool for randomized trials (RoB2):¹⁹ up to two RoB2 assessments for each study, for each method of data collection. Disagreements were resolved through discussion and with consultation with a third reviewer (AW-H).

The RoB ratings were compared across studies in which IPD, AD or no data were available.

Patient and public involvement and engagement

We held meetings with service users prior to application as part of our process for finalising proposed methods. We also set up a formal Service User Advisory Group (SUAG) comprising young people: service users with a personal experience of self-harm, aged 14–16. Input from this group led to changes to our original plain language summary and dissemination plans. Importantly, the SUAG, while acknowledging that the data might not always be available recommended that we look at the impact of LGBT status, ethnicity, ASD status, and learning difficulty status in relation to response to psychological treatments for self-harm. This was then included in our design.

We held regular meetings with the SUAG during the study to inform them on the progress and discuss emerging issues. We will be meeting with them again now that analysis is completed to discuss dissemination and next steps.

Equality, diversity and inclusion

The University of Leeds is fully committed to equality, diversity and inclusion. As a secondary data study, this

review did not include any research participants. We were fully inclusive in all the studies we reviewed and reported on and, with our search strategy, tried to ensure that key studies were not missed. We tried to ensure our PPIE group members were as inclusive of disadvantaged groups as was possible.

Our PPIE group were instrumental in ensuring that in our review we looked specifically for the possibility that being a part of a disadvantaged or underserved group might increase the risk of a poor outcome.

Results

Study selection and individual participant data obtained

Our PRISMA diagram ([Figure 1](#)) sets out the numbers of records identified at different stages of the search and the IPD received. We identified and screened 3690 unique records related to 3610 studies up to 21 January 2022. These were identified from our direct searches for RCTs, our harvesting of RCTs from systematic reviews and from checking the reference lists of identified eligible RCTs. Title and abstract screening resulted in 366 records relating to 286 studies for full-text screening, of which 73 studies met our inclusion criteria.

Of these 73 studies, the full sample of recruited participants met our eligibility criteria for 18 studies, while only part of the sample were eligible for 11 studies due to age (only some participants being aged 16–18 years) or prior self-harm status (only some participants had previously self-harmed), and 44 studies required further enquiries to establish eligibility. Contact with authors led to 10 further studies confirmed as including a partial sample of eligible participants. A further 20 were confirmed as ineligible, and 2 were ongoing studies. In 12 cases, it was not possible to confirm eligibility; we were unable to trace authors in 9 cases, and in 3, the data were no longer available to establish eligibility. The 2 ongoing and 12 unconfirmed studies excluded at this stage are summarised in [Appendix 3](#) (from search paper).

Thus, at the end of this stage, we identified 39 studies, where we sought IPD, of which the full sample of participants were eligible in 18 studies, comprising 2383 eligible participants, and a partial sample of participants were eligible in 21 studies, comprising approximately 2217 eligible participants.

The timetable for sending out requests for DSAs and IPD sets is summarised in [Table 2](#).

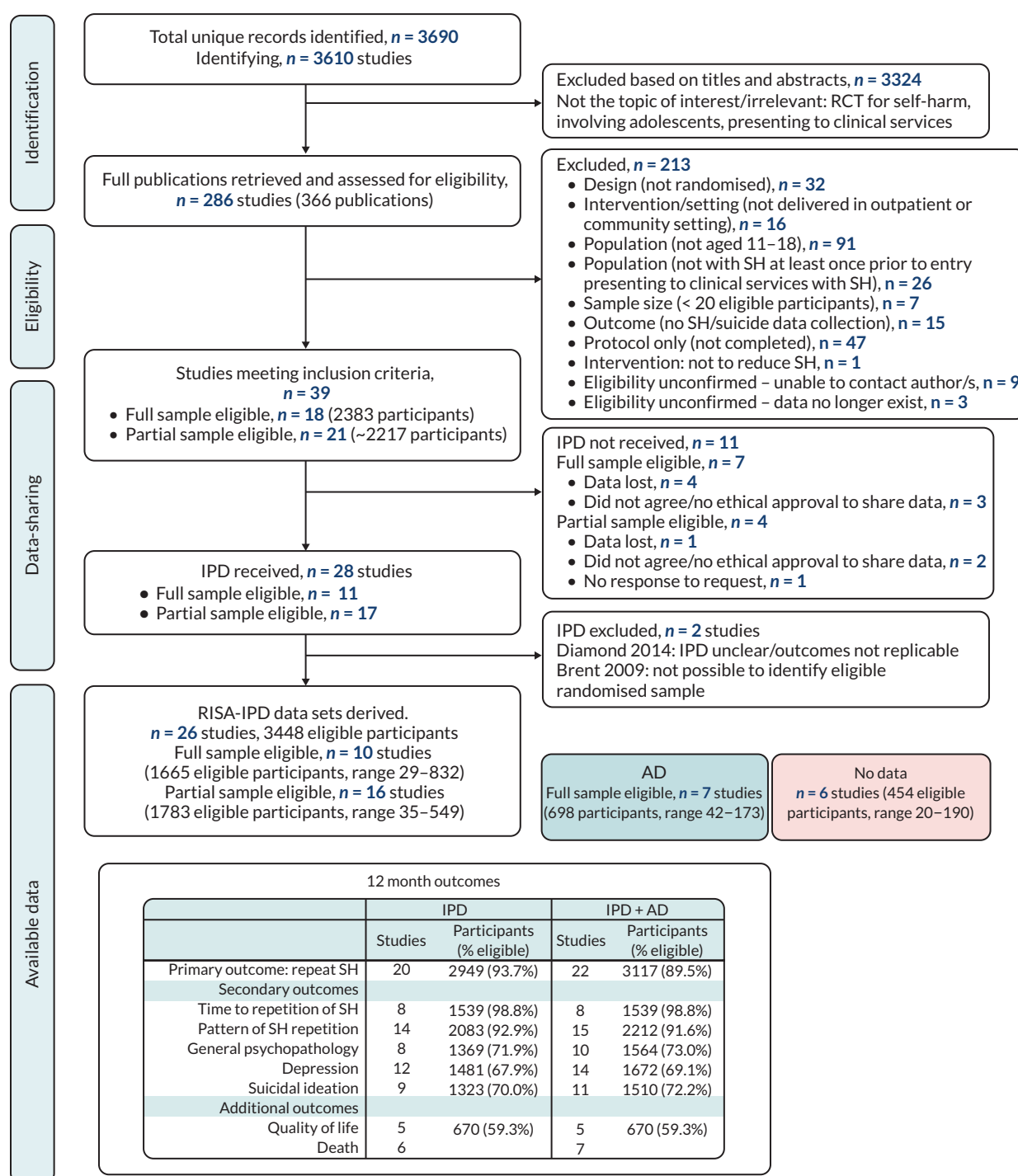


FIGURE 1 The PRISMA flow chart.

We obtained DSAs and IPD in 28 (72%) of the 39 studies. Of the 18 full sample eligible studies, we obtained agreement for 11 (61%) studies and were informed that data sets for 4 were lost (all studies conducted before 2005). For one study, the author was clear that their original ethical approval did not allow for data-sharing; and in two others, the authors were concerned about permission to share and the possibility of participant identification. Of the 21 partial sample eligible studies, we obtained agreement for

17 (81%) studies. The data set was lost for one study; in another, the author was clear that their original ethical approval did not allow for data-sharing, and in another, the author was concerned about permission to share and the possibility of participant identification. We had no response to requests for data from the final study author.

Individual participant data were cleaned and verified on receipt, and data were harmonized in May 2020

and finished in March 2022. We excluded two studies from our final analysis during the process of cleaning and verification. One was an unpublished pilot with insufficient data to reliably derive the variables we needed for our study. The second was designed as an RCT, but recruitment difficulties led to a halt in randomisation after 22 participants had been recruited; from that point, participants could choose their intervention. The 22 randomised participants were eligible for our study, but although the full data set was available, it proved impossible to identify the randomised subsample.

Thus, we concluded this stage of the review with IPD from 26/39 (66.7%) of eligible studies, providing data for 3448/4600 (75%) eligible participants (Figures 2 and 3). These included: 10/18 (55.6%) studies, in which the full study sample was eligible providing data for a total of 1665/2383 (69.9%) eligible participants (range 29–832); and 16/21 (76.2%) studies, where a partial sample of study participants was eligible, providing data for a total 1783/2217 (80.4%) additional eligible participants (range 35–549).

In addition, published AD from seven of the full sample eligible studies were included in our secondary IPD plus aggregate meta-analysis (contributing an additional 698 participants, range 42–173).

In the five studies where a partial sample was eligible, but AD were not available, we estimated 434 eligible, randomised, participants from the total 914 participants, but without IPD, it was not possible to confirm exactly how many participants would have been eligible, or include the participants in IPD or AD sets.

TABLE 2 The DSA and IPD request timeline

Date	Action
August 2019	First literature search
October 2019	First request for DSAs sent out
October 2019	First DSA received
May 2020	First request for IPD sent out
June 2020	First set of IPD received
December 2020	Final DSA received
May 2021	Final set of IPD received
March 2022	All data queries resolved; final database synthesised

This synopsis should be referenced as follows:

Cottrell D, Walwyn R, Farrin A, Irving D, Fonagy P, Ougrin D, et al. Reducing self-harm in adolescents: the RISA-IPD comprehensive synopsis. *Health Technol Assess* 2026;30(3):1–52. <https://doi.org/10.3310/KKBB1164>

Study characteristics

Table 3 provides an overview of study characteristics. Studies were conducted across a wide range of countries and interventions. The majority of studies evaluated effectiveness (76.9%) as opposed to pilot or feasibility (23.1%) and were 2-arm RCTs (87.2%) with three 2-arm Zelen RCTs, one 2-arm cluster RCT and one 3-arm RCT/patient preference design. Of studies providing IPD, most participants were female (2823, 82.0%) with mean (SD) age 15.7 (SD = 1.6) years.

Table 4 provides a comparison of study characteristics for studies with and without IPD. A greater proportion of studies without IPD was from the USA (61.5%) compared to studies that did provide IPD (26.9% from the USA), and studies without IPD tended to have been published earlier (median 13 vs. 10 years). IPD were obtained for all studies rated as low RoB overall, with a greater proportion of studies rated as high RoB where IPD were not obtained (38.5% vs. 11.5%).

Risk of bias within and across studies

Risk-of-bias assessment outputs are summarised in Figure 4. For the primary outcome, repetition of self-harm, six studies were rated as low RoB,^{25,43,48,49,59,67} all of which provided IPD. Eight studies were rated as high risk,^{32,33,35,36,38,40,62,66} three of which provided IPD, and two AD. The small number of low-risk studies was largely because most outcomes were via self-report from non-blinded participants (Domain 4), and most trials did not have pre-specified, published, analysis plans (Domain 5).

The RISA primary self-harm outcome was collected using health records in 13 studies (either alone or in combination with self-report), of which 6 studies were rated as low RoB (see above), 5 as showing some concerns, and 2 were rated as high RoB.^{33,36} Ten of these studies also collected secondary outcomes via self-report/interview; none remained as low risk when RoB ratings were made for secondary outcomes.

Studies where we did not have IPD tended to be rated as showing more concerns (see Table 4), with the larger differences being in Domain 4, measurement of the outcome (42% rated low risk if we had IPD; 8% rated low risk if not), Domain 5, selection of the reported result (31% vs. 0%), and overall RoB (23% vs. 0%).

Domain 1: Bias arising from randomisation process

Most trials were rated as low risk in this domain (33/39, 85%). Three trials were rated as being of high risk: in two^{32,66}, there were differences in baseline scores and insufficient

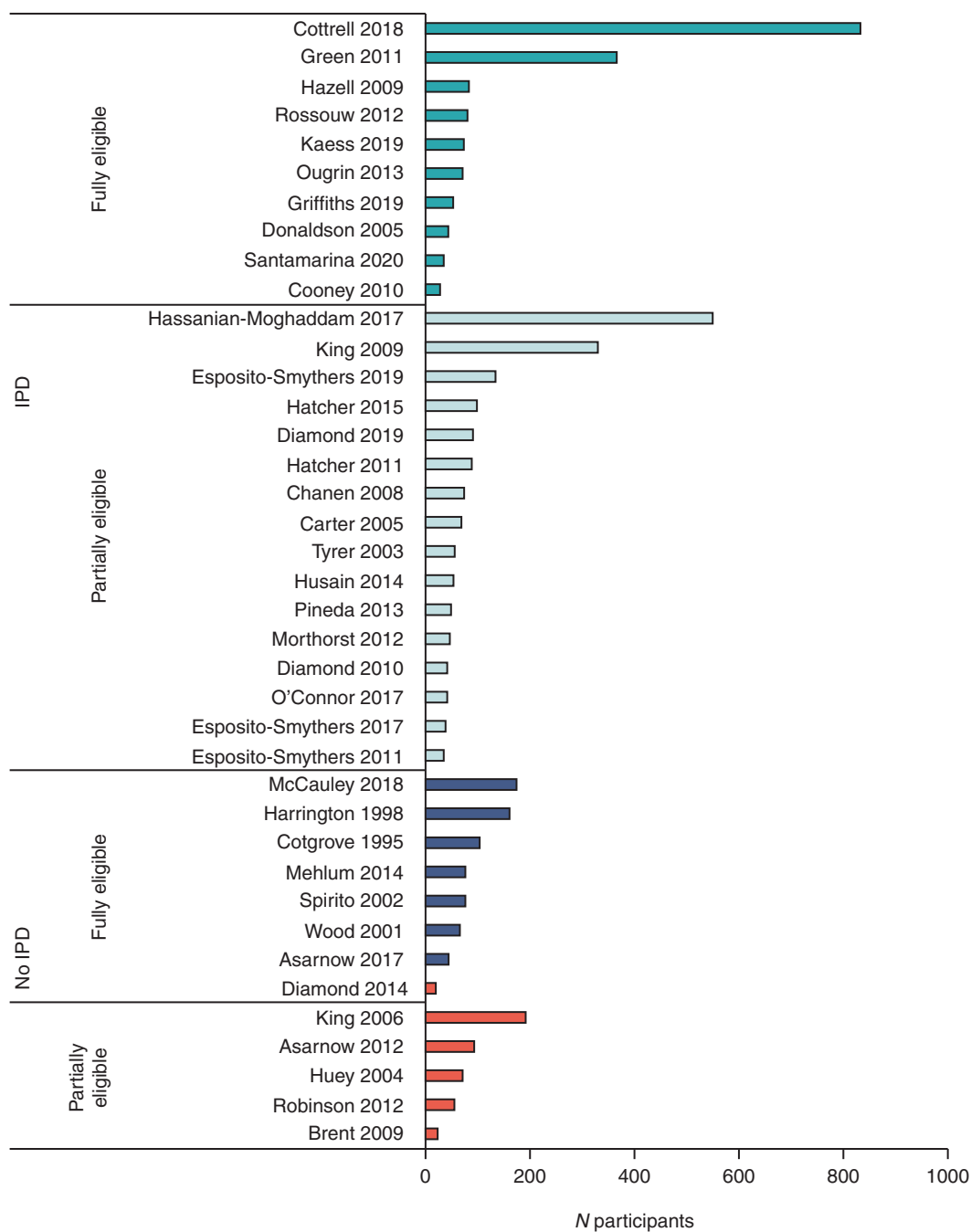


FIGURE 2 Eligible studies, sample sizes and data availability.

information about allocation concealment. In the third,³⁶ there was insufficient information about allocation concealment and baseline differences post randomisation.

For those rated as some concern, one had insufficient information about allocation concealment,⁴⁰ two had some differences in baseline scores suggesting problems with randomisation^{34,45} and one had insufficient information about baseline differences post randomisation.³⁸

Domain 2: Bias due to deviations from intended interventions

Most trials (33/39, 85%) were rated as low risk as there was little evidence of deviation from the intended assigned intervention, and ITT analyses were used. Four trials were rated as high RoB: two reported deviations in the intended intervention (Carter *et al.*³³ 20, control participants received the intervention in error; Cooney *et al.* 2010:³⁵ per protocol analyses were undertaken); in one

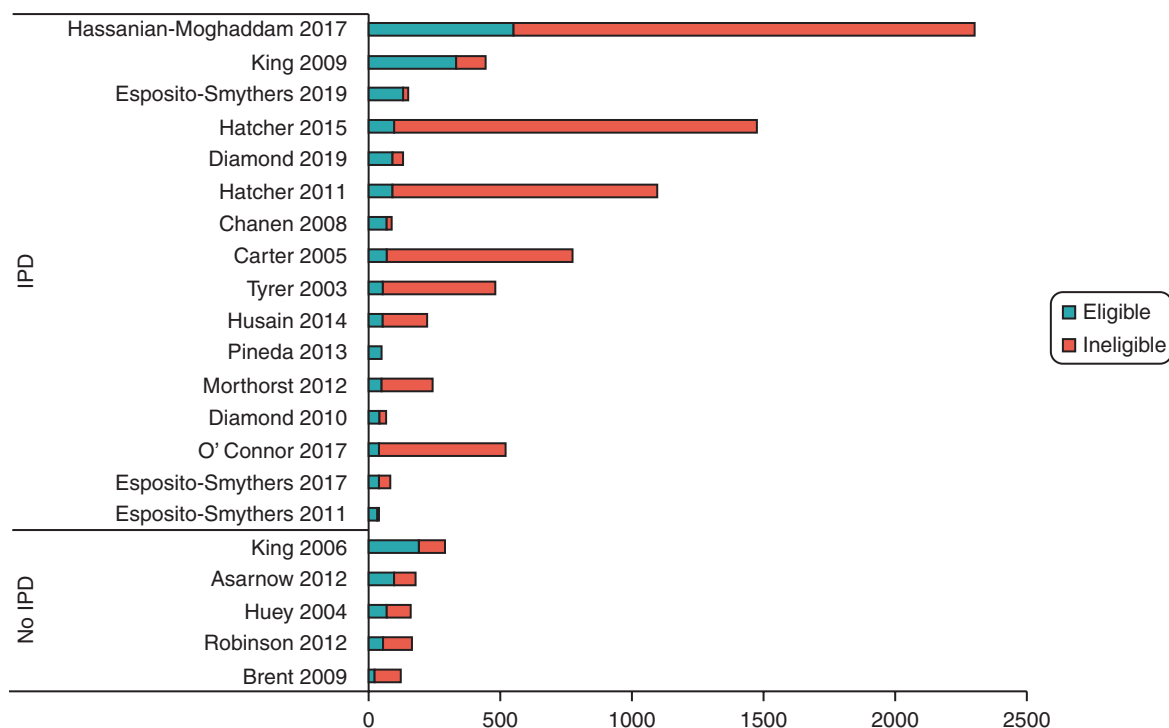


FIGURE 3 Eligible participants in partial sample eligible studies.

study, there was insufficient information about possible deviations from the intended assigned intervention or about the ITT analysis plan.³⁸ One study⁴⁰ was originally rated as low risk in this domain, but examination of the IPD supplied showed that there were 44 participants initially randomised, not the 39 reported in the trial publication. Original analysis was therefore not ITT, and the rating was changed to high risk.

Two trials were rated as having some concerns; in one,⁵⁴ there was insufficient information about possible deviations from the intended assigned intervention, and in the other,⁶⁶ there was insufficient information about the ITT analysis plan.

Domain 3: Bias due to missing outcome data

Three trials were rated as high risk: one trial³⁸ had insufficient information about availability of outcome data, and one⁶² had high levels of missing data rated likely to depend on the true value of the missing data. The third trial⁴⁰ was originally rated as low risk, but examination of the IPD supplied showed that there were 44 participants initially randomised, not the 39 reported in the trial publication. Data on these participants were not available and likely to be related to outcome, as they were excluded

due to lack of compliance with the intended intervention. The rating was therefore changed to high risk.

Two trials that collected our primary and secondary outcomes using different methods were rated as high risk for self-reported secondary outcomes. Morthorst *et al.* (2012),⁵⁸ where more data were missing from the control group than the intervention group, and Tyrer *et al.* (2003),⁶⁷ where data from both arms were missing; in both cases, the missing data were likely to depend on the true value of that data. Both were rated as low risk with respect to RISA-IPD primary outcome data collected through hospital records.

Ten trials were rated as having some concerns.^{25,42,48,49,51,54,55,60,65,66} In each case, this was because of missing outcome data, but with missingness rated as unlikely to be related to the true value of the data, or, where appropriate, analysis methods were used to account for missing data. The exception was Huey *et al.* (2004),⁵¹ where there was insufficient information to know if acceptable levels of outcome data had been collected.

Five trials in this group^{25,48,49,60,65} were rated as having some concerns for self-reported secondary outcome data only, and as of low risk in the same domain on our

TABLE 3 Characteristics of included studies

Study	Data available ^a	Country	Design	Aim ^b	Study powered	Total sample size (eligible)	Eligibility	Mean age	Female (%)	Intervention	Control group ^c	Treatment intensity	Treatment duration (weeks)	N treatment sessions	Any group element in treatment	Any family element in treatment	Method of SH data collection ^d	Overall RoB
Asarnow 2011 ³⁰	No Data	USA	2-arm RCT	Effectiveness	Yes	181	Partial	14.7	69	CBT	TAU	Low	4	5	No	Yes	Self-report	Some concerns
Asarnow 2017 ³¹	Aggregate	USA	2-arm RCT	Pilot	No	42	Full	14.6	88.1	CBT	Enhanced TAU	Medium	12	10	No	Yes	Self-report	Some concerns
Brent 2009 ³²	No Data	USA	3-arm RCT/preference	Pilot	No	124 (22 randomised)	Partial	15.7	77.4	CBT	Active	High	26	24	No	Yes	Self-report	High
Carter 2007 ³³	IPD	Australia	2-arm Zelen RCT	Effectiveness	Yes	772 (68 aged 11-18)	Partial	17.6	82.4	Postcards/tokens	TAU	Low	52	0	No	No	Medical records	High
Chanen 2008 ³⁴	IPD	Australia	2-arm RCT	Effectiveness	Yes	86 (72 prior SH)	Partial	16.4	79.2	CAT/MBT	Enhanced TAU	High	24	24	No	No	Self-report	Some concerns
Cooney 2010 ³⁵	IPD	New Zealand	2-arm RCT	Pilot	No	29	Full	16	75.9	DBT	TAU	High	26	52	Yes	Yes	Self-report	High
Cotgrove 1995 ³⁶	Aggregate	UK	2-arm RCT	Effectiveness	No	105	Full	14.9	84.8	Postcards/tokens	TAU	Low	0	0	No	No	Medical records	High
Cottrell 2018 ²⁵	IPD	UK	2-arm RCT	Effectiveness	Yes	832	Full	14.8	88.6	FT	TAU	Medium	26	8	No	Yes	Medical records	Low
Diamond 2010 ³⁷	IPD	USA	2-arm RCT	Effectiveness	No	66 (41 prior SH)	Partial	15	92.7	FT	Enhanced TAU	Medium	12	12	No	Yes	Self-report	Some concerns
Diamond 2014 ³⁸	No Data	USA	2-arm RCT	Pilot	No	20	Full	14.9	80	FT	Enhanced TAU	.	16	16	No	Yes	Self-report	High
Diamond 2019 ³⁹	IPD	USA	2-arm RCT	Effectiveness	Yes	129 (90 with prior SH)	Partial	15	84.4	FT	Active	Medium	16	16	No	Yes	Self-report	Some concerns
Donaldson 2005 ⁴⁰	IPD	USA	2-arm RCT	Pilot	No	44	Full	14.9	79.5	PST	Active	Medium	26	10	No	Yes	Self-report	High
Esposito-Smythers 2011 ⁴¹	IPD	USA	2-arm RCT	Pilot	No	40 (35 prior SH)	Partial	15.7	65.7	CBT	Enhanced TAU	High	52	54	No	Yes	Self-report	Some concerns
Esposito-Smythers 2017 ⁴²	IPD	USA	2-arm RCT	Pilot	No	81 (37 prior SH)	Partial	15.5	67.6	CBT	Enhanced TAU	Medium	4	3	Yes	Yes	Self-report	Some concerns

TABLE 3 Characteristics of included studies (continued)

Study	Data available ^a	Country	Design	Aim ^b	Study powered	Total sample size (eligible)	Eligibility	Mean age	Female (%)	Intervention	Control group ^c	Treatment intensity	Treatment duration (weeks)	N treatment sessions	Any group element in treatment	Any family element in treatment	Method of SH data collection ^d	Overall RoB
Esposito-Smythers 2019 ⁴³	IPD	USA	2-arm RCT	Effectiveness	Yes	147 (133 prior SH)	Partial	14.8	79.7	CBT	Enhanced TAU	High	52	54	No	Yes	Combined approach	Low
Green 2011 ⁴⁴	IPD	UK	2-arm RCT	Effectiveness	Yes	366	Full	15.1	88.5	GT	TAU	Medium	6	10	Yes	No	Self-report	Some concerns
Griffiths 2019 ⁴⁵	IPD	UK	2-arm RCT	Pilot	No	53	Full	15.5	79.2	CAT/MBT	TAU	Medium	12	12	Yes	No	Medical records	Some concerns
H-Moghaddam 2017 ⁴⁶	IPD	Iran	2-arm RCT	Effectiveness	Yes	2300 (549 aged 11–18)	Partial	16.7	74.3	Postcards/tokens	TAU	Low	12	0	No	No	Self-report	Some concerns
Harrington 1998 ⁴⁷	Aggregate	UK	2-arm RCT	Effectiveness	Yes	162	Full	14.5	89.5	FT	TAU	Medium	.	5	No	Yes	Self-report	Some concerns
Hatcher 2011 ⁴⁸	IPD	New Zealand	2-arm Zelen RCT	Effectiveness	Yes	1094 (89 aged 11–18)	Partial	18.3	67.4	CBT	TAU	Medium	12	9	No	No	Medical records	Low
Hatcher 2015 ⁴⁹	IPD	New Zealand	2-arm Zelen RCT	Effectiveness	Yes	1474 (98 aged 11–18)	Partial	17.8	77.6	CBT	TAU	Medium	52	8	No	No	Medical records	Low
Hazell 2009 ⁵⁰	IPD	Australia	2-arm RCT	Effectiveness	No	82	Full	14.5	90.2	GT	TAU	Medium	6	6	Yes	No	Self-report	Some concerns
Huey 2004 ⁵¹	No data	USA	2-arm RCT	Effectiveness	No	156 (70 with prior SH)	Partial	12.9	35	MST	Active	High	16	.	No	Yes	Self-report	Some concerns
Husain 2014 ⁵²	IPD	Pakistan	2-arm RCT	Effectiveness	Yes	221 (53 aged 11–18)	Partial	17.4	77.4	PST	TAU	Medium	12	6	No	No	Self-report	Some concerns
Kaess 2019 ⁵³	IPD	Germany	2-arm RCT	Effectiveness	Yes	74	Full	14.9	95.9	CBT	TAU	Medium	16	12	No	No	Self-report	Some concerns
King 2006 ⁵⁴	No Data	USA	2-arm RCT	Effectiveness	No	289 (190 prior SH)	Partial	15.3	68.2	PST	TAU	Medium	26	26	No	Yes	Self-report	Some concerns
King 2009 ⁵⁵	IPD	USA	2-arm RCT	Effectiveness	No	448 (331 prior SH)	Partial	15.6	73.1	PST	TAU	Medium	12	12	No	Yes	Self-report	Some concerns

continued

TABLE 3 Characteristics of included studies (continued)

Study	Data available ^a	Country	Design	Aim ^b	Study powered	Total sample size (eligible)	Eligibility	Mean age	Female (%)	Intervention	Control group ^c	Treatment intensity	Treatment duration (weeks)	N treatment sessions	Any group element in treatment	Any family element in treatment	Method of SH data collection ^d	Overall RoB
McCauley 2018 ⁵⁶	Aggregate	USA	2-arm RCT	Effectiveness	Yes	173	Full	14.9	94.8	DBT	Active	High	26	52	Yes	Yes	Self-report	Some concerns
Mehlum 2014 ⁵⁷	Aggregate	Norway	2-arm RCT	Effectiveness	Yes	77	Full	15.6	88.3	DBT	Enhanced TAU	High	19	38	Yes	Yes	Medical records	Some concerns
Morthorst 2012 ⁵⁸	IPD	Denmark	2-arm RCT	Effectiveness	Yes	243 (46 aged 11–18)	Partial	16.1	95.7	PST	TAU	Medium	26	20	No	Yes	Medical records	Some concerns
O'Connor 2017 ⁵⁹	IPD	UK	2-arm RCT	Effectiveness	Yes	518 (39 aged 11–18)	Partial	17.2	74.4	Postcards/tokens	TAU	Low	8	1	No	No	Medical records	Low
Ougrin 2013 ⁶⁰	IPD	UK	2-arm cluster-RCT	Effectiveness	Yes	70	Full	15.6	80	Brief intervention	TAU	Low	1	1	No	Yes	Medical records	Some concerns
Pineda 2013 ⁶¹	IPD	Australia	2-arm RCT	Effectiveness	Yes	48 (48 with prior SH ^e)	Partial	15.1	79.2	PST	TAU	Medium	8	4	No	Yes	Self-report	Some concerns
Robinson 2012 ⁶²	No Data	Australia	2-arm RCT	Effectiveness	Yes	164 (~56 aged 11–18 prior SH)	Partial	18.6	64.6	Postcards/tokens	TAU	Low	52	0	No	No	Self-report	High
Rossouw 2012 ⁶³	IPD	UK	2-arm RCT	Effectiveness	Yes	80	Full	15.1	85	CAT/MBT	TAU	High	52	64	No	Yes	Self-report	Some concerns
Santamarina 2017, 2020 ^{64,65}	IPD	Spain	2-arm RCT	Effectiveness	No	35	Full	15.3	88.6	DBT	Active	High	16	40	Yes	Yes	Combined approach	Some concerns
Spirito 2002 ⁶⁶	Aggregate	USA	2-arm RCT	Effectiveness	No	76	Full	15	90	Brief intervention	TAU	Low	8	5	No	Yes	Self-report	High
Tyrer 2003 ⁶⁷	IPD	UK	2-arm RCT	Effectiveness	Yes	480 (54 aged 11–18)	Partial	17.8	88.9	CBT	TAU	Medium	12	7	No	No	Combined approach	Low

TABLE 3 Characteristics of included studies (continued)

Study	Data available ^a	Country	Design	Aim ^b	Study powered	Total sample size (eligible)	Eligibility	Mean age	Female (%)	Intervention	Control group ^c	Treatment intensity	Treatment duration (weeks)	N treatment sessions	Any group element in treatment	Any family element in treatment	Method of SH data collection ^d	Overall RoB
Wood 2001 ⁶⁸	Aggregate	UK	2-arm RCT	Pilot	No	63	Full	14.2	78	GT	TAU	Medium	26	26	Yes	No	Self-report	Some concerns

a The reasons IPD were not provided or excluded were: the data had been lost and were no longer available for Cotgrove *et al.* 1995,³⁶ Harrington *et al.* 1998,⁴⁷ Spirito *et al.* 2002,⁶⁶ Wood *et al.* 2001⁶⁸ and King *et al.* 2006;⁵⁴ authors did not agree to share data or felt they did not have ethical approval to share for Asarnow *et al.* 2011,³⁰ Asarnow *et al.* 2017,³¹ McCauley *et al.* 2018,⁵⁶ Mehlum *et al.* 2014,⁵⁷ and Robinson *et al.* 2012;⁶² there was no response to our request for Huey *et al.* 2004;⁵¹ IPD were obtained but excluded for the unpublished Diamond 2014³⁸ study as the IPD were not consistent with limited aggregate results detailed in the list of excluded studies in the Hawton *et al.* 2015¹⁷ review; and IPD were obtained but excluded for Brent 2009 as eligible participants could not be identified.

b Pilot studies include pilot or feasibility studies.

c TAU = treatment as usual; E-TAU = enhanced treatment as usual; active = active control.

d Self-report includes researcher interview; medical records include hospital records, studies that collected the primary outcome using a combination of methods primarily relied on self-report verified by medical record.

e Pineda and Dadds 2013⁶¹; partially eligible as eligibility based on suicidal behaviour, including ideation only; however, authors confirmed all met RISA eligibility criteria. IPD did not include the RISA primary outcome (AD also unavailable).

TABLE 4 Study characteristics by data availability^a

	IPD (n = 26)	Aggregate (n = 7)	No data (n = 6)	Total (n = 39)
Eligibility				
Full sample eligible	10 (38.5%)	7 (100.0%)	1 (16.7%)	18 (46.2%)
Partial eligible	16 (61.5%)	0 (0.0%)	5 (83.3%)	21 (53.8%)
N eligible participants				
Mean (SD)	132.6 (187.54)	99.7 (50.06)	75.7 (63.06)	117.9 (156.68)
Median (range)	69.0 (29–832)	77.0 (42–173)	63.0 (20–190)	70.0 (20–832)
Total	3448	698	454	4600
Age (years)				
Weighted mean	15.7	14.8	15.4	15.5
Range (of study means)	14.5–18.3	14.2–15.6	12.9–18.6	12.9–18.6
SD	1.6	–	–	–
Female (%)				
Weighted mean	82.0	88.9	63.7	79.6
Range (of study means)	65.7–95.9	78.0–94.8	35.0–80.0	35.0–95.9
Years since primary publication				
Mean (SD)	9.3 (4.79)	15.3 (9.89)	12.7 (3.78)	10.9 (6.18)
Median (range)	10.0 (2.0–19.0)	20.0 (4.0–27.0)	12.0 (8.0–18.0)	11.0 (2.0–27.0)
Country				
USA	7 (26.9%)	3 (42.9%)	5 (83.3%)	15 (38.5%)
Rest of world	19 (73.1%)	4 (57.1%)	1 (16.7%)	24 (61.5%)
Pilot/feasibility or effectiveness trial				
Pilot/feasibility	5 (19.2%)	2 (28.6%)	2 (33.3%)	9 (23.1%)
Effectiveness	21 (80.8%)	5 (71.4%)	4 (66.7%)	30 (76.9%)
Study powered				
No	9 (34.6%)	4 (57.1%)	4 (66.7%)	17 (43.6%)
Yes	17 (65.4%)	3 (42.9%)	2 (33.3%)	22 (56.4%)

TABLE 4 Study Characteristics by data availability (*continued*)

	IPD (n = 26)	Aggregate (n = 7)	No data (n = 6)	Total (n = 39)
RISA intervention				
CBT	7 (26.9%)	1 (14.3%)	2 (33.3%)	10 (25.6%)
DBT	2 (7.7%)	2 (28.6%)	0 (0.0%)	4 (10.3%)
FT	3 (11.5%)	1 (14.3%)	1 (16.7%)	5 (12.8%)
GT	2 (7.7%)	1 (14.3%)	0 (0.0%)	3 (7.7%)
CAT/MBT	3 (11.5%)	0 (0.0%)	0 (0.0%)	3 (7.7%)
MST	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (2.6%)
PST	5 (19.2%)	0 (0.0%)	1 (16.7%)	6 (15.4%)
Postcards/tokens	3 (11.5%)	1 (14.3%)	1 (16.7%)	5 (12.8%)
Brief intervention	1 (3.8%)	1 (14.3%)	0 (0.0%)	2 (5.1%)
RISA control group				
TAU	18 (69.2%)	4 (57.1%)	3 (50.0%)	25 (64.1%)
Enhanced TAU	5 (19.2%)	2 (28.6%)	1 (16.7%)	8 (20.5%)
Active	3 (11.5%)	1 (14.3%)	2 (33.3%)	6 (15.4%)
Treatment intensity				
Low	4 (15.4%)	2 (28.6%)	2 (33.3%)	8 (20.5%)
Medium	16 (61.5%)	3 (42.9%)	1 (16.7%)	20 (51.3%)
High	6 (23.1%)	2 (28.6%)	2 (33.3%)	10 (25.6%)
Unknown	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (2.6%)
Treatment duration (weeks)				
Mean (SD)	21.3 (16.77)	15.2 (10.40)	23.3 (16.23)	20.6 (15.70)
Median (range)	14.0 (1–52)	15.5 (0–26)	21.0 (4–52)	16.0 (0–52)
Number of treatment sessions				
Mean (SD)	17.1 (18.95)	19.4 (19.71)	14.2 (11.45)	17.2 (17.95)
Median (range)	10.0 (0–64)	10.0 (0–52)	16.0 (0–26)	10.0 (0–64)

continued

TABLE 4 Study Characteristics by data availability (continued)

	IPD (n = 26)	Aggregate (n = 7)	No data (n = 6)	Total (n = 39)
Group element in treatment (yes) ^a	6 (23.1%)	3 (42.9%)	0 (0.0%)	9 (23.1%)
Family element in treatment (yes) ^a	14 (53.8%)	5 (71.4%)	5 (83.3%)	24 (61.5%)
Method of data collection: self-harm^d				
Self-report/researcher interview	15 (57.7%)	5 (71.4%)	6 (100.0%)	26 (66.7%)
Hospital/medical records	8 (30.8%)	2 (28.6%)	0 (0.0%)	10 (25.6%)
Combined approach	3 (11.5%)	0 (0.0%)	0 (0.0%)	3 (7.7%)
Overall RoB				
Low	6 (23.1%)	0 (0.0%)	0 (0.0%)	6 (15.4%)
Some concerns	17 (65.4%)	5 (71.4%)	3 (50.0%)	25 (64.1%)
High	3 (11.5%)	2 (28.6%)	3 (50.0%)	8 (20.5%)

a Characteristics marked with^a were investigated in subgroup and meta-regression to explore study-level sources of between-study heterogeneity on treatment effect estimates.

b For partially eligible studies with IPD, the mean age and percentage of females are for the eligible sample; otherwise, data are for the full recruited sample. Participants with IPD range in age from 11 to 18.9 years.

c Seven studies (26.9%) were conducted in the USA, seven (26.9%) in Australasia, seven (26.9%) in the UK, three (11.5%) elsewhere in Europe, and two (7.7%) in Asia. Additional AD for seven studies included three US studies, three UK studies and one study in Norway.

d Meta-regression based on: primary outcome data collection self-report (inc. combined) vs. medical records.

primary outcome where data were collected through hospital records.

Domain 4: Bias in measurement of the outcome

For our primary outcome, twelve trials^{25,33,43,45,48,49,57-60,65,67} were rated as being of low RoB where measurement of

the outcome was via, or verified by, hospital or medical records. No studies were rated as being at high RoB, with the remainder typically rated as having some concerns, as measurement of outcomes was by self-report alone and participants were aware of allocation status. For self-reported secondary outcomes, all studies were rated as having some concerns.

Review ^a	Study ID	Experimental	Comparator	Outcome	D1	D2	D3	D4	D5	Overall
Full sample eligible, IPD included										
1	Cooney 2010	DBT	TAU	4	+	-	+	!	!	-
1 ^a	Cottrell <i>et al.</i> 2018	FT	TAU	1	+	+	+	+	+	+
2 ^a	Cottrell <i>et al.</i> 2018	FT	TAU	5	+	+	!	!	+	!
1	Donaldson 2005	PST	Active control	4	!	-	-	!	!	-
1	Green 2011	GT	TAU	4	+	+	+	!	!	!
1 ^a	Griffiths 2019	MBT/CAT	TAU	1	!	+	+	+	!	!
2 ^a	Griffiths 2019	MBT/CAT	TAU	5	!	+	+	!	!	!
1	Hazell 2009	GT	TAU	4	+	+	+	!	!	!
1	Kaess 2019	CBT	TAU	4	+	+	+	!	+	!
1 ^a	Ougrin 2013	Brief intervention	TAU	1	+	+	+	+	+	!
2 ^a	Ougrin 2013	Brief intervention	TAU	5	+	+	!	!	!	!
1	Rossouw 2012	MBT/CAT	TAU	4	+	+	+	!	!	!
1 ^a	Santamarina 2020	DBT	Active control	3	+	+	+	+	!	!
2 ^a	Santamarina 2020	DBT	Active control	5	+	+	!	!	!	!
Full sample eligible, IPD excluded, AD not available										
1	Diamond 2014	FT	Enhanced TAU	4	!	-	-	!	-	-
Full sample eligible, IPD not provided, AD available										
1	Asarnow 2017	CBT	Enhanced TAU	4	+	+	+	!	!	!
1	Cotgrove 1995	Postcards/tokens	TAU	1	-	+	+	!	!	-
1	Harrington 1998	FT	TAU	4	+	+	+	!	!	!
1	McCauley 2018	DBT	Active control	4	+	+	+	!	!	!
1 ^a	Mehlum 2014	DBT	Enhanced TAU	1	+	+	+	!	!	!
2 ^a	Mehlum 2014	DBT	Enhanced TAU	5	+	+	+	!	!	!
1	Spirito 2002	Brief intervention	TAU	2	-	!	!	!	!	-
1	Wood 2001	GT	TAU	4	+	+	+	!	!	!
Partial sample eligible, IPD included										
1	Carter <i>et al.</i> 2005	Postcards/tokens	TAU	1	+	-	+	!	!	-
1	Chanen 2008	MBT/CAT	Enhanced TAU	4	!	+	+	!	!	!
1	Diamond 2010	FT	Enhanced TAU	4	+	+	+	!	!	!
1	Diamond 2019	FT	Active control	4	+	+	+	!	!	!
1	Esposito-Smythers 2011	CBT	Enhanced TAU	4	+	+	+	!	!	!
1	Esposito-Smythers 2017	CBT	Enhanced TAU	4	+	+	!	!	!	!
1 ^a	Esposito-Smythers 2019	CBT	Enhanced TAU	3	+	+	+	+	+	+
2 ^a	Esposito-Smythers 2019	CBT	Enhanced TAU	5	+	+	+	!	+	!
1	Hassanian 2017	Postcards/tokens	TAU	2	+	+	+	!	!	!
1 ^a	Hatcher 2011	CBT	TAU	1	+	+	+	+	+	+
2 ^a	Hatcher 2011	CBT	TAU	5	+	+	!	!	+	!
1 ^a	Hatcher 2015	CBT	TAU	1	+	+	+	+	+	+
2 ^a	Hatcher 2015	CBT	TAU	5	+	+	!	!	+	!
1	Husain 2014	PST	TAU	4	+	+	+	!	+	!
1	King 2009	PST	TAU	4	+	+	!	!	!	!
1 ^a	Morthorst 2012	PST	TAU	1	+	+	+	+	!	!
1 ^a	Morthorst 2012	PST	TAU	5	+	+	-	!	!	-
1	O'Connor 2017	Postcards/tokens	TAU	1	+	+	+	+	+	+
1	Pineda 2013	PST	TAU	4	+	+	+	!	!	!
1 ^a	Tyrer 2003	CBT	TAU	3	+	+	+	+	+	+
2 ^a	Tyrer 2003	CBT	TAU	5	+	+	-	!	+	-
Partial sample eligible, IPD excluded, AD not available										
1	Brent 2009	CBT	TAU	4	-	+	+	!	!	-
Partial sample eligible, IPD not provided, AD not available										
1	Asarnow 2011	CBT	TAU	4	+	+	+	!	!	!
1	Huey 2004	MST	Active control	4	+	+	!	!	!	!
1	King 2006	PST	TAU	4	+	!	!	!	!	!
1	Robinson 2012	Postcards/tokens	TAU	4	+	+	-	!	!	-

+ Low risk
! Some concerns
- High risk

RoB domain

D1 Randomisation process
 D2 Deviations from the intended interventions
 D3 Missing outcome data
 D4 Measurement of the outcome
 D5 Selection of the reported result

Outcome

1 SH outcome/s via hospital/medical records
 2 SH outcome/s via self-report/interview
 3 SH outcome/s via hospital/medical records and self-report/interview
 4 All outcomes via self-report/interview
 5 Other outcomes via self-report/interview

Intervention

CBT - Cognitive Behavioural Therapy
 DBT - Dialectical Behaviour Therapy
 Family Therapy
 Group Therapy
 MBT/CAT - Metabolisation, Psychodynamic, Cognitive Analytic Therapy
 MST - Multisystemic Therapy
 PST - Problem solving, psychoeducation, support
 Postcard/tokens - postcards, tokens, documents
 Brief intervention - other single-session, brief intervention

FIGURE 4 Summary of RoB ratings. a, These studies collected the RISA-IPD primary outcome of self-harm from health records, and other secondary outcome data (i.e. depression, suicidal ideation, general psychopathology) using different methods through interview or selfreport. Two RoB assessments were carried out, one for each data collection method. The first rating is for the RISA-IPD primary outcome of self-harm collected via health records. The second rating is for other secondary outcome data.

This synopsis should be referenced as follows:
 Cottrell D, Walwyn R, Farrin A, Irving D, Fonagy P, Ougrin D, *et al.* Reducing self-harm in adolescents: the RISA-IPD comprehensive synopsis. *Health Technol Assess* 2026;30(3):1-52.
<https://doi.org/10.3310/KKBB1164>

Domain 5: Bias in selection of the reported result

Across outcomes, only eight studies^{25,43,48,49,52,53,59,67} were rated as low risk on this domain. One study³⁸ was rated as being at high RoB, with the remainder rated as having some concerns. In almost all cases, this was because of a lack of a published, detailed, pre-specified analysis plan, either in the form of a published protocol paper with analysis plan, or with a detailed analysis plan in the trial registration.

Results of syntheses

Summary statistics and step 1 treatment effect estimates for each outcome for individual studies are contained within [Report Supplementary Material 4](#), along with forest plots and funnel plots for all step 2 analysis, and sensitivity analyses.

To illustrate overall pooled treatment effect estimates, forest plots depicting secondary combined IPD and AD meta-analysis of 12-month outcomes are presented within the synopsis ([Figures 5 and 6](#)), as these represent analyses containing the greatest number of studies (see also [Report Supplementary Material 4, Figures 1–25](#)). Forest plots depicting primary IPD meta-analysis of participant moderator effects are presented within the synopsis ([Figures 7–9](#)) and in [Report Supplementary Material 4](#) (see [Figures 26, 27, 34, 35, 37–39](#) for key findings).

Overall pooled treatment effects

Primary outcome: repetition of self-harm

Our analysis found no evidence that interventions were more or less effective than controls at reducing repeat self-harm at 12 months in IPD meta-analysis (OR 1.06, 95% CI 0.86 to 1.31,) of 2949 (93.7% eligible) participants from 20 studies or IPD + AD meta-analysis (OR 1.02, 95% CI 0.82 to 1.27) of 3117 (89.5% eligible) participants from 22 studies ([Figure 5; Report Supplementary Material 4, Figure 3](#)). Due to high levels of variability in outcome within studies, between-study heterogeneity was relatively low, and there was no evidence of heterogeneity in treatment effects between groups of interventions. Similarly, there was no evidence that interventions overall were more or less effective than control at 3, 6, 18, 24 or > 24 months or for heterogeneity between interventions; all CIs included the null effect and spanned both meaningful small positive and negative effects ([Report Supplementary Material 4, Figures 1–6](#)).

Except CBT at 12 months, most intervention-specific pooled effect estimates were based on four or fewer studies, and there was no evidence that any were more or less effective than control at reducing repeat self-harm

at any time period. The 6-month pooled treatment effect for DBT showed the most promising positive effect in IPD + AD meta-analysis of 276 participants from four studies, with a comparatively tight CI compared to other interventions (OR 0.54, 95% CI 0.22 to 1.32). However, there was insufficient evidence to detect a statistically significant reduction, and the upper bound included clinically meaningful negative effects.

There was no evidence of between-study heterogeneity in treatment effects, except at the 10% level for the two to three studies of GT (IPD $I^2 = 72.2%$, $p = 0.058$; IPD + AD $I^2 = 76.2%$, $p = 0.015$) at 12 months; and between two IPD studies of CBT at 18 months ($I^2 = 71.7%$, $p = 0.06$) and CAT/MBT at 3 months ($I^2 = 64.6%$, $p = 0.093$) in which contrasting treatment effects were observed.

Time to repetition of self-harm

Our analyses found no evidence that interventions were more or less effective than control on time-to-repetition overall or by intervention, with data from 1539 (98.8% eligible) participants from eight studies with IPD ([Report Supplementary Material 4, Figure 10](#)). Median follow-up was 43 months (range 0–82.5 months) and ranged from 6 to 60 months across studies. There was no evidence of between-study heterogeneity overall or by intervention, or heterogeneity between groups of interventions.

Pattern of self-harm repetition

Our analyses found no evidence that interventions (overall or by intervention) were more or less effective than controls at reducing self-harm between 6 and 12 months in IPD meta-analysis of 2083 (92.9% eligible) participants from 14 studies, or in IPD + AD meta-analysis of 2212 (91.6% eligible) participants from 15 studies ([Report Supplementary Material 4, Figure 7](#)). There was similarly no evidence on outcomes at 12–18 months, 18–24 months or beyond 24 months; all CIs included the null effect and spanned mainly small effects overall, and small to large effects by intervention ([Report Supplementary Material 4, Figures 7–9](#)).

Overall, between-study heterogeneity was low, and there was no evidence of heterogeneity between groups of interventions; however, there was some indication of between-study heterogeneity for two GT studies with contrasting effects at 6–12 months (IPD $I^2 = 69.0%$, $p = 0.072$; IPD + AD $I^2 = 67.1%$, $p = 0.081$), and two CBT studies at 12–18 months in IPD meta-analyses ($I^2 = 64.9%$, $p = 0.092$).

General psychopathology

There was good evidence of a small positive effect, indicating that interventions were more effective

than control at reducing general psychopathology at 12 months in IPD meta-analysis (SMD -0.13 , 95% CI -0.25 to -0.01) of 1369 (71.9% eligible) participants from eight studies, and IPD + AD meta-analysis (SMD -0.13 , 95% CI -0.25 to -0.02) of 1564 (73.0% eligible) participants from 10 studies (*Report Supplementary Material 4, Figure 13*). Overall intervention effects were consistent but not statistically significant at other time points (*Report Supplementary Material 4, Figures 11–14*). Between-study heterogeneity was low, and there was no evidence of heterogeneity between groups of interventions at 12 months. There was evidence of between-study heterogeneity in the overall treatment effect in IPD but not IPD + AD meta-analyses at 3 months due to the large treatment effect observed for one study of PST in adjusted analysis; and 6 months due to larger treatment effect estimates observed for one DBT and one PST study.

In meta-analysis comparing specific interventions to control, there was insufficient evidence to detect a statistically significant reduction in general psychopathology; and there was some evidence of between-study heterogeneity for two GT studies with IPD ($I^2 = 67.0\%$, $p = 0.082$) at 12 months but not when a further study with AD was added. There was evidence of a reduction in general psychopathology for specific interventions compared to control in IPD meta-analysis, but only when estimates were based on single studies: PST at 3 and 6 months; DBT at 6 months, but not when including two additional studies with AD; and CBT at 18 months.

Depression

Our analyses found no evidence that therapeutic interventions were more or less effective than controls at reducing depression in IPD meta-analyses of 1481 (67.9% eligible) participants from 12 studies, or IPD + AD meta-analyses of 1672 (69.1% eligible) participants from 14 studies at 12 months, or other time points (*Report Supplementary Material 4, Figures 15–18*). All CIs included the null effect and spanned mainly small (positive and negative) effects overall, and small to large effects by intervention.

There was no evidence of heterogeneity between groups of interventions. There was statistical evidence of between-study heterogeneity in the overall treatment effect at 18 months, driven by conflicting effect estimates between two studies of CBT. There was also evidence of heterogeneity between two studies of FT at 3 months and some evidence at 6 months, but in IPD meta-analysis only, and between three studies of PST at 6 months in IPD meta-analysis only.

Suicidal ideation

Our analyses found no evidence that therapeutic interventions were more or less effective than control at reducing suicidal ideation at 12 months in IPD meta-analysis of 1323 (70.0% eligible) participants from 9 studies, or IPD + AD meta-analysis of 1510 (72.2% eligible) participants from 11 studies (*Report Supplementary Material 4, Figure 21*). There was no evidence of between-study heterogeneity, or heterogeneity between groups of interventions. There was similarly no evidence that any intervention (overall or by intervention) was more or less effective than control at 3 or 18 months (*Report Supplementary Material 4, Figures 19 and 22*).

Evidence of a small positive effect of intervention compared to control was observed on 6-month suicidal ideation in IPD + AD meta-analysis (SMD -0.17 , 95% CI -0.32 to -0.02) of 1418 participants from 15 studies; however, this effect was not supported by IPD meta-analysis with fewer studies (2 DBT, 1 FT) (*Report Supplementary Material 4, Figure 20*). The positive overall effect observed was driven largely by small to moderate effects in DBT (SMD -0.43 , 95% CI -0.90 to 0.03) involving 258 participants from four studies, CBT (SMD -0.24 , 95% CI -0.90 to 0.42) involving 170 participants from three studies, and FT (SMD -0.15 , 95% CI -0.95 to 0.65) involving 261 participants from three studies.

There was some evidence of heterogeneity between the FT studies at 6 months in IPD meta-analysis but not IPD + AD meta-analysis, including an additional study. There was also evidence of heterogeneity between groups of interventions at 6 months in IPD + AD meta-analysis ($p = 0.094$) driven by the range of effects observed for DBT, CBT and FT, and null effects found for GT and PST.

Assessment of publication bias and small study effect

Funnel plots showed no evidence of small study effects or publication bias, with a few exceptions (*Report Supplementary Material 4, Figures 23 and 24*). Outlying studies with positive treatment effects and a lack of symmetry were observed for IPD + AD meta-analysis of general psychopathology at 6 and 12 months. Pooled treatment effect estimates from one-stage fixed-effect IPD meta-analysis (more robust to small study bias) were comparable to random-effects IPD meta-analysis at 12 months but attenuated the treatment effect at 6 months.

Lack of symmetry was observed for IPD + AD meta-analysis of depression at 6 and 12 months (Egger's test $p = 0.024$ and $p = 0.101$, respectively), and IPD + AD meta-analysis of suicidal ideation at 3 and 6 months (Egger's

test $p = 0.063$ and $p = 0.021$, respectively). However, lack of symmetry was less pronounced for adjusted IPD meta-analysis, and one-stage fixed-effect and two-stage random-effect IPD meta-analysis were comparable for both outcomes.

Sensitivity analysis

There were few notable differences in results and no changes to conclusions from sensitivity analyses using multiple imputation (*Report Supplementary Material 4, Figures 1–22*), one-stage random or fixed-effects IPD meta-analysis, or IPD + AD meta-analysis excluding studies of high RoB.

Two-stage IPD meta-analysis with multiple imputation gave similar results overall and by intervention compared with primary complete-case analysis except for 3-month depression outcomes for FT interventions, where there was a reduction in the magnitude of the pooled treatment effect estimate and between-study heterogeneity (*Report Supplementary Material 4, Figure 13*).

One-stage random-effect IPD meta-analysis gave similar pooled treatment effect estimates (where estimation was possible) compared to the primary two-stage approach, with generally wider CIs both overall and by intervention.

One-stage fixed-effect IPD meta-analysis resulted in pooled treatment effect estimates which were generally comparable or closer to the null with tighter CIs compared with estimates obtained in primary random-effects IPD meta-analyses. On the primary outcomes, pooled treatment effect estimates were closer to the null (no effect) for GT at 6 and 12 months, and CBT at 18 months, where the greatest level of between-study heterogeneity were observed. On secondary outcomes, there were few changes to conclusions, except for general psychopathology, where smaller CIs for fixed-effect estimates provided significant evidence that interventions overall and GT interventions were more effective than control at 6 months, as were GT interventions at 12 months.

Additional sensitivity analysis of two-stage IPD + AD meta-analysis was conducted for the pattern of self-harm outcome to explore the impact of zero events in one arm; estimates were largely comparable and no change to conclusions.

Additional outcomes

There was no evidence that interventions were more or less effective than controls on improving quality of life at 12 months in individual studies involving 670 (59.3% eligible) participants from 5 studies with IPD and no studies with AD at 12 months (*Report Supplementary Material 4, Table 8*).

Adolescent deaths were reported for 11 eligible participants in 7 studies and for 2 participants in 2 partially eligible studies where eligibility could not be determined (*Report Supplementary Material 4, Table 9*). No eligible participants died in 10 studies, and no deaths were reported in the remaining 20 studies.

Study and treatment moderators

There was no statistical evidence of between-study heterogeneity in treatment effect on the primary outcome when all interventions were compared with control at any time point. In IPD + AD meta-analyses, heterogeneity was estimated to be 0 at all time points, with exception of 12 ($I^2 = 12.1%$, 95% CI 0 to 48.2%, studies = 22) and 18 months ($I^2 = 14%$, 95% CI 0 to 66.8%, studies = 6). Given the lack of heterogeneity and small number of studies, subgroup analyses and metaregression were conducted only at 12 months. No candidate study or treatment-level moderators were found to be significantly associated with treatment effect (see Figure 5c; *Report Supplementary Material 4, Table 9 and Figure 25*).

Adolescent moderators

Age and gender were the only baseline characteristics available in all 26 studies with IPD. Most participants were female (2823/3448, 82.0%), with mean age 15.7 (SD = 1.6) years. In 18 (69.2%) studies reporting ethnicity, over three-quarters of participants were White (1947/2482, 78.4%).

In 15 (57.7%) studies, over half of the participants (1138/1989, 57.2%) were reported as depressed based on clinical review using a structured tool, and just under three-quarters exhibited suicidal ideation (1620/2221, 72.9%). In 14 (53.8%) studies, just over half of the participants (917/1682, 54.5%) were diagnosed with a clinical anxiety disorder or indicated by questionnaire. In seven (26.9%) studies, including all 3 studies of CAT/MBT, 163 out of 921 (17.7%) participants were clinically diagnosed with BPD. Family dysfunction was indicated in 747/966 (77.3%) participants from four (15.4%) studies, and 325/2198 participants (14.8%) from 12 (46.2%) studies were on psychotropic medication at baseline.

In 21 (80.8%) studies, over half of the participants had self-harmed multiple times (1874/3213, 59.3%), and of 14 (53.8%) studies reporting the method of self-harm, 1471/2779 (52.9%) presented prior to or at trial participation with self-poisoning, 1052 (37.9%) with self-injury, and 245 (8.8%) used a combination. Data on the outcome or severity of participants' prior self-harm were available in 18 (69.2%) studies, but due to considerable variability in data collection, synthesis of these data was not carried out.

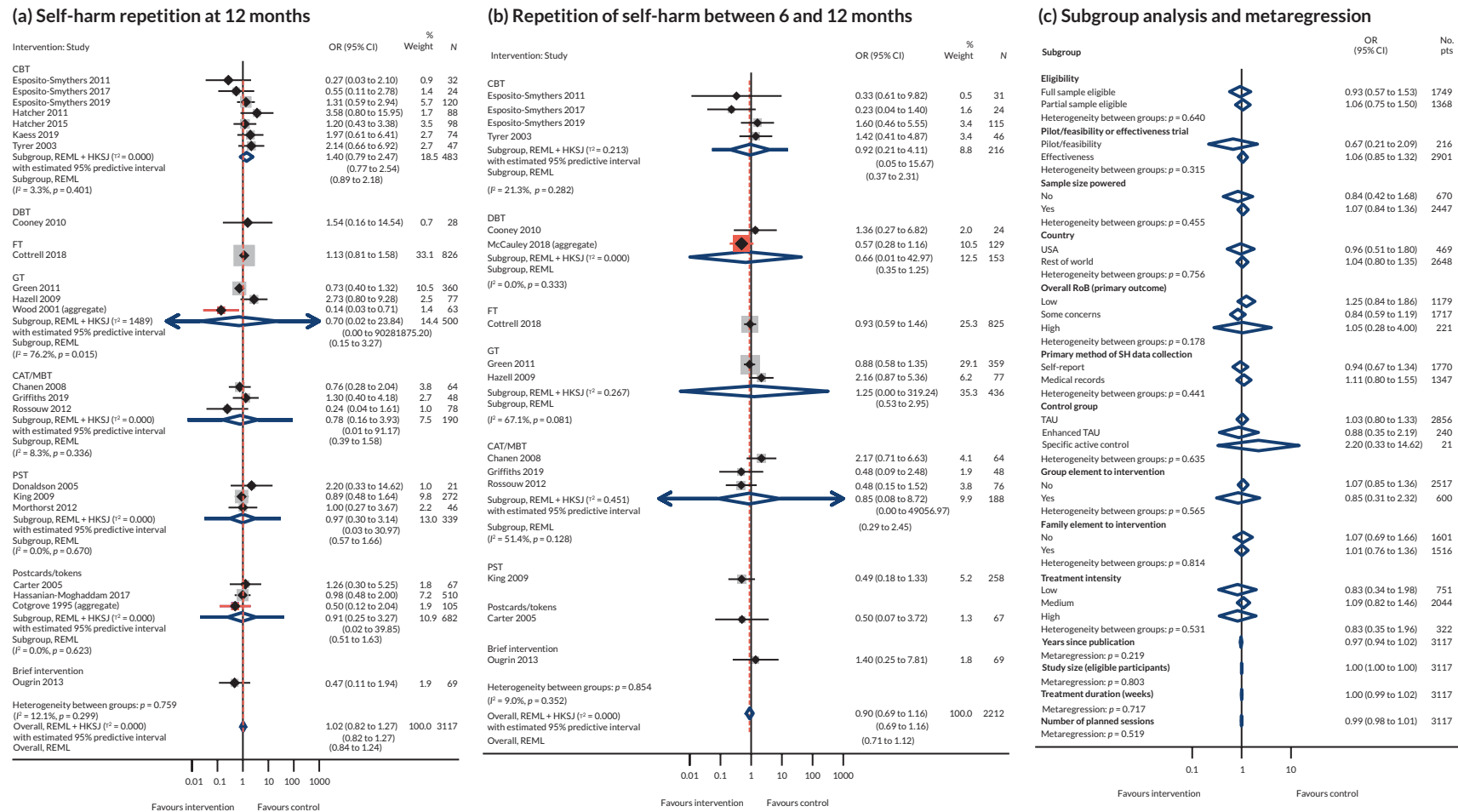


FIGURE 5 Forest plot of the effects for intervention vs. control on the (a) primary outcome self-harm repetition at 12 months, (b) secondary outcome repetition of self-harm between 6 and 12 months and (c) primary outcome – meta-regression. Note: Secondary unadjusted IPD + AD meta-analysis. Colour coding is to highlight studies where estimates are from AD in orange. The x-axis presents the OR.

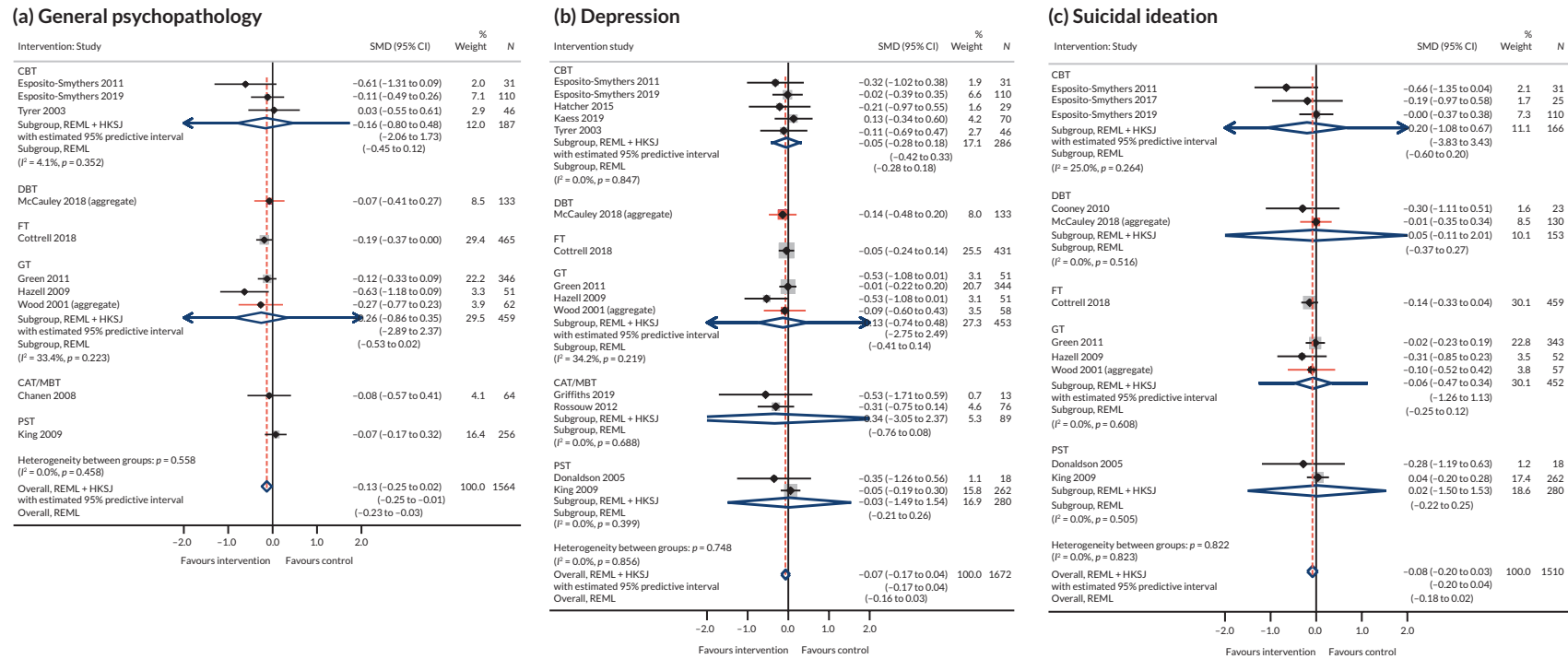


FIGURE 6 Forest plot of the effects for intervention vs. control on 12-month secondary outcomes (a) general psychopathology, (b) depression and (c) suicidal ideation. Note: Secondary unadjusted IPD + AD meta-analysis. Colour coding is to highlight studies where estimates are from AD in orange. The x-axis presents the SMD.

While family dysfunction and psychotropic medication was available in fewer than half of the studies, these were explored further alongside additional moderators, as data were available in all three FT studies. Other baseline characteristics available in fewer than half of the studies included unemotional and callous traits, LGBTQ status, ASD, abuse, presence of an eating disorder, intellectual disability looked after children, and presence of a physical health problem.

Effect of age on treatment effects

Our IPD meta-analysis found no evidence that interventions were either more or less effective than controls in reducing repeat self-harm based on participants' age, with data from 2447 out of 2590 (94.5% eligible) participants in 21 studies at 6 months and 2948 out of 3142 (93.8% eligible) participants in 20 studies at 12 months (see [Figure 7a](#); [Report Supplementary Material 4](#), [Figure 26](#)). While the overall pooled moderator effect suggested an improved treatment effect for older participants, this was not statistically significant, and a reversed effect was observed on repeated self-harm between 6 and 12 months.

As seen in the estimation of the overall pooled effects, due to considerable variability within studies, variability between studies was comparatively low. There was no evidence of heterogeneity between studies and no indication that age moderated the treatment effect on repetition of self-harm outcomes in specific interventions. However, the pooled moderator effects for CBT and PST showed more positive effects for older participants, whereas GT showed beneficial effects for younger participants.

On secondary outcomes general psychopathology, depression, and suicidal ideation ([Report Supplementary Material 4](#), [Figure 27](#)), there were small yet consistent moderator effects suggesting a slightly better treatment outcome for older participants on. However, in 12-month general psychopathology outcomes, there was some evidence of variability between studies ($I^2 = 49.2\%$, $p = 0.055$) and heterogeneity among different interventions ($p = 0.015$). This was primarily influenced by single study effects showing a better treatment response in older participants in PST, CBT and CAT/MBT, compared to a tendency for improved outcomes in younger participants in a single FT study.

In secondary analysis, CIs without the HKSJ adjustment indicated a more effective treatment for older participants in PST, observed at 6 months on repetition of self-harm (OR 0.56, 95% CI* 0.26 to 0.90) in 400 participants from four studies and on suicidal ideation (SMD -0.19, 95% CI* -0.36 to -0.03) in 319 participants from three studies ([Figure 7b](#); [Report Supplementary Material 4](#), [Figure 27](#)).

Effect of gender on treatment effects

Our analysis found no evidence for a difference in the treatment effect on reducing repeat self-harm based on gender, with data from 2401 out of 2590 (92.7% eligible) participants across 21 studies at 6 months and 2828 out of 3142 (90% eligible) participants from 20 studies at 12 months. Nor was there evidence for a gender-based difference in the treatment effect on secondary outcomes ([Report Supplementary Material 4](#), [Figures 28 and 29](#)).

On self-harm repetition outcomes, there was no evidence of variability between studies or heterogeneity among different groups of interventions, nor within groups of interventions, except for two GT studies with contrasting effects (6 months $I^2 = 75.5\%$, $p = 0.043$; 12 months $I^2 = 73.8\%$, $p = 0.051$). There was evidence of variability between studies on 6-month general psychopathology outcomes across all studies ($I^2 = 47.9\%$, $p = 0.062$) and again in two GT studies on both 6-month general psychopathology ($I^2 = 75.6\%$, $p = 0.043$) and 6-month depression outcomes ($I^2 = 65.1\%$, $p = 0.09$) as influenced by an enhanced treatment effect observed in female participants in a single GT study.

Confidence intervals, when not adjusted with the HKSJ method, showed an improved treatment effect in male compared to female participants for depression outcomes in CBT at 6 months (SMD -0.70, 95% CI* -1.39 to -0.02) in 190 participants from three studies, and 12 months (SMD -0.69, 95% CI* -1.39 to -0.0) in 216 participants from four studies ([Figure 8](#); [Report Supplementary Material 4](#), [Figures 28 and 29](#)).

Effect of clinical depression diagnosis and level of depression on treatment effects

Analysis revealed no evidence for a difference in the treatment effect based on whether participants had received a clinical diagnosis of depression, or participants' level of depression in terms of reducing repeated self-harm, or on secondary outcomes ([Report Supplementary Material 4](#), [Figures 30–33](#)).

In most analyses, there was no evidence of variability between studies, heterogeneity among different groups of interventions, or variability within groups of interventions. Based on participants' clinical depression diagnosis, there was some evidence of variability between studies on 6-month depression outcomes in two GT studies ($I^2 = 69.7\%$, $p = 0.069$). Based on participants' level of depression, there was also some evidence of heterogeneity among different groups of interventions on 12-month depression outcomes ($p = 0.062$); some evidence

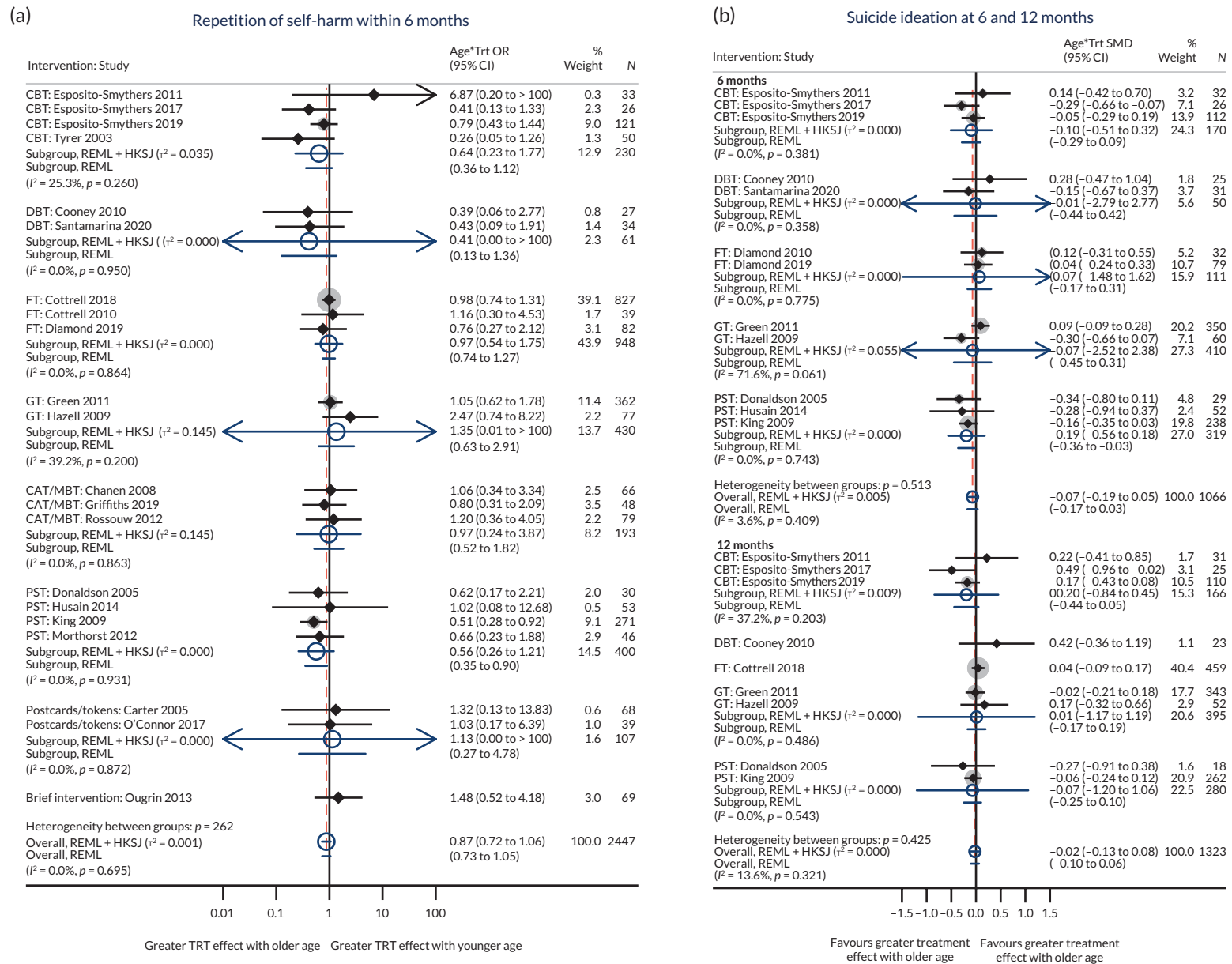


FIGURE 7 Forest plot of the differential effects for intervention vs. control, according to participants' age on (a) repetition of self-harm within 6 months and (b) suicide ideation at 6 and 12 months. a, The x-axis presents the OR; b, The x-axis presents the SMD.

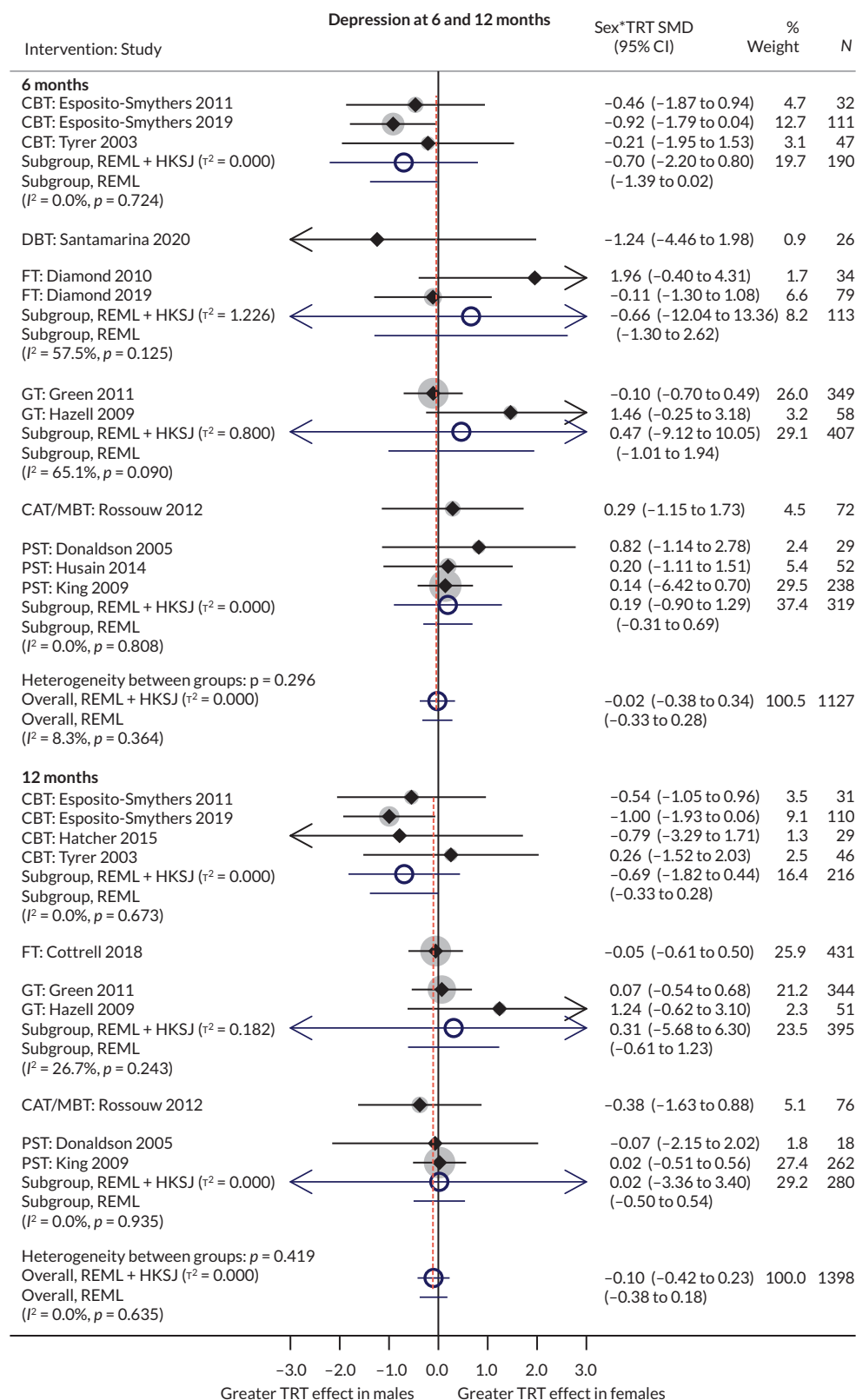


FIGURE 8 Forest plot of the differential effects for intervention vs. control, according to participants' gender on depression. Note: The x-axis presents the SMD.

of variability on 6-month general psychopathology ($I^2 = 60.4\%$, $p = 0.08$) outcomes and depression outcomes ($I^2 = 62.9\%$, $p = 0.044$), between three and four CBT studies, respectively; and some evidence of variability between studies for 6-month suicide ideation outcomes in three PST studies ($I^2 = 63.9\%$, $p = 0.063$).

Effect of self-harm method on treatment effects

We found no evidence that interventions were more or less effective than controls based on participants' method of self-harm on reducing repeat self-harm or secondary outcomes (see [Report Supplementary Material 4, Figures 34 and 35](#)). While there was an overall trend towards a more positive treatment outcome for participants presenting with self-poisoning compared to self-injury, particularly on self-harm repetition at 6 months (OR 0.70, 95% CI 0.27 to 1.76) in 1673 participants from 6 studies, and suicidal ideation at 12 months (SMD -0.23 , 95% CI -0.74 to 0.28) in 1109 participants from four studies, this was not statistically significant.

There was no evidence of variability between studies overall or within specific groups of interventions on self-harm outcomes. There was evidence of heterogeneity among different groups of interventions regarding 6–12-month self-harm repetition ($p = 0.078$), due to contrasting single study effects in FT and PST. There was also evidence of variability between studies on suicidal ideation outcomes, particularly at 6 months across all three studies ($I^2 = 82.6\%$, $p = 0.003$), and in two GT studies (6 months $I^2 = 81.1\%$, $p = 0.021$; 12 months $I^2 = 68.0\%$, $p = 0.077$), due to an outlying trend towards an improved treatment effect in participants with self-injury in one GT study.

Effect of borderline personality disorder on treatment effects

There was no evidence for a difference in the treatment effect on reducing repeat self-harm or secondary outcomes based on whether participants were diagnosed with BPD ([Report Supplementary Material 4, Figure 36](#)). No studies were available to investigate the moderating effect of BPD on suicidal ideation.

In most analyses, there was no evidence of variability between studies, heterogeneity among different groups of interventions, or variability within groups of interventions. There was some evidence of variability on 12-month depression outcomes, overall between four studies ($I^2 = 53.3\%$, $p = 0.092$) and in two CBT studies ($I^2 = 72.1\%$, $p = 0.058$) due to a more pronounced treatment effect in participants with BPD in a single CBT study with a high RoB.

Effect of number of prior self-harm episodes on treatment effects

We found evidence of a more favourable treatment effect in participants with multiple previous self-harm episodes compared to those with fewer (≤ 2) on the secondary outcome repetition of self-harm within 6–12 months (OR 0.33, 95% CI 0.12 to 0.94) in 1771 participants from 9 studies ([Figure 9](#)). This interaction should be considered alongside the overall treatment effect, which showed a non-significant 7% reduction in the likelihood of repeat self-harm in intervention versus control [OR 0.93 (95% CI 0.71 to 1.23), studies = 14; [Report Supplementary Material 4, Figure 7a](#)]. A more favourable, but not statistically significant, treatment effect was similarly indicated in participants with multiple previous self-harm episodes on primary repeat self-harm outcomes at 6 and 12 months, general psychopathology and suicidal ideation outcomes, and on 12- but not 6-month depression outcomes (see [Report Supplementary Material 4, Figures 37 and 38](#)). There was no evidence of variability between studies, heterogeneity among different groups of interventions, or variability within groups of interventions across all outcomes.

Additional moderators

While there was no evidence of a difference in treatment effect based on whether participants had an anxiety disorder in terms of reducing repeat self-harm, there was a consistent trend suggesting a more favourable treatment effect for those with clinically or questionnaire indicated anxiety (see [Report Supplementary Material 4, Figure 39](#)). This was particularly noticeable at 12 months (OR 0.74, 95% CI 0.33 to 1.66) in 1226 participants from 10 studies, especially in 5 studies of CBT (OR 0.40, 95% CI 0.06 to 2.62) involving 322 participants. There was no evidence of variability between studies, heterogeneity among different groups of interventions, or variability within groups of interventions.

There was no evidence of a difference in treatment effect on reducing repeated self-harm based on participants' level of family dysfunction, ethnicity, use of psychotropic medication, or whether participants exhibited suicidal ideation or the severity of their ideation; and no evidence of variability between studies, heterogeneity among groups of interventions, or variability within groups of interventions in these analyses ([Report Supplementary Material 4, Figures 40–44](#)).

There was some evidence of variability between two studies based on family dysfunction at 12 months ($I^2 = 69.0\%$, $p = 0.072$), driven by contrasting treatment effects in single studies of FT and PST.

There was strong evidence of variability between two GT studies based on participants' level of suicidal ideation (6 months $I^2 = 82.0\%$, $p = 0.019$; 12 months $I^2 = 80.8\%$, $p = 0.022$) due to a detrimental treatment effect in participants with, or with higher levels of, suicidal ideation in one study but not the other.

Assessment of publication bias and small study effect

Funnel plots for all moderators and outcomes, and regression-based Egger's tests, generally indicated no evidence of small study effects or publication bias ([Report Supplementary Material 4, Figure 45](#)). The notable exception

was the moderating effect of the level of depression on the primary outcome at 12 months, where some evidence of bias was observed ($p = 0.0638$).

Additional analysis

In analysis where CIs for combined treatment effects were calculated without the HKSJ adjustment, results appeared more precise due to the exclusion of uncertainty in estimated between-study heterogeneity. This change in methodology did not result in any differences in overall conclusions. The only exceptions were the moderating effects of age on the repetition of self-harm and suicidal

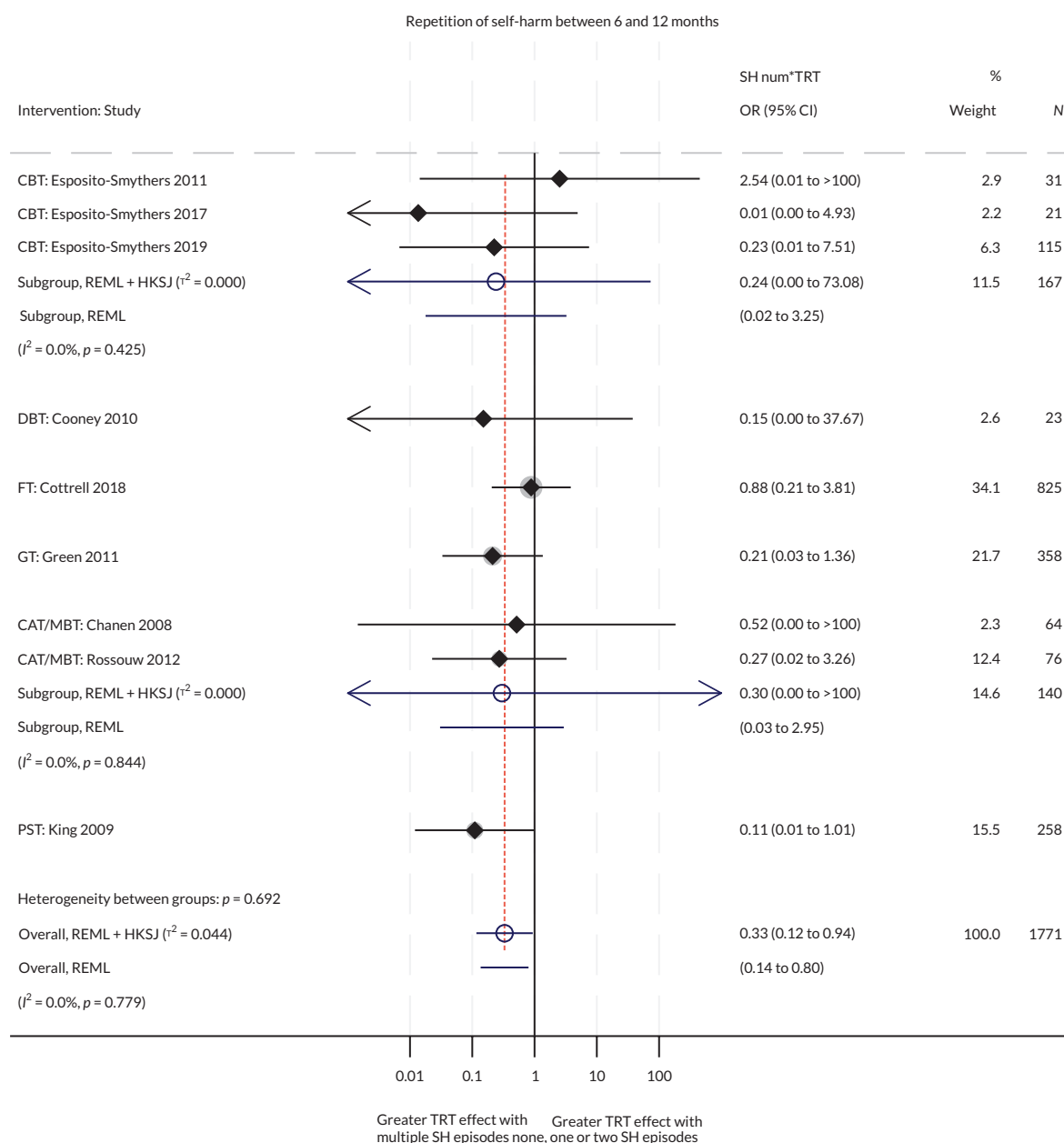


FIGURE 9 Forest plot of the differential effects for intervention vs. control, according to participants' number of self-harm episodes on repetition of self-harm between 6 and 12 months. Note: The x-axis presents the OR. See [Report Supplementary Material 4](#) for associated subgroup effects.

ideation within 6 months in PST, and the effect of gender on depression outcomes at both 6 and 12 months.

Discussion

Summary and interpretation of findings

Our IPD meta-analysis of studies evaluating interventions for self-harm in adolescents has had three main components. First, we reported on the search methods we used, the process of identifying eligible studies and the assessment of RoB. Second, we reported on our primary analysis of the effectiveness of interventions to prevent repetition of self-harm and other outcomes. Finally, we explored potential individual participant moderators that might have influenced outcomes for subgroups of adolescents.

Following our searches, we identified 39 studies that met our inclusion criteria. Of these, in 18 studies the full sample were eligible, and in a further 21, a part of the sample was eligible. In this latter group, the main reasons for partial sample eligibility were age, not all the sample were 18 years old or under, and lack of evidence of self-harm prior to randomisation, that is, some participants were included in the original studies because of suicidal ideation only.

Of the 39 studies, we obtained IPD in 28 (72%); IPD were no longer available, or there were ethical concerns about sharing data in studies which did not provide IPD. Two of the 28 studies were then excluded. In one unpublished pilot study, there were insufficient data to derive the variables we needed for our study. In the second, it proved impossible to identify the randomised subsample from the data available in the data depository.

The final IPD analysis therefore included 26 studies with 3448 eligible participants: 10 studies in which the full study sample was eligible (1665 participants), and 16 studies where a partial sample was eligible (1783 participants). We were also able to include AD on 698 participants from seven full sample eligible studies where IPD were not provided in our secondary IPD plus aggregate meta-analysis.

The data collection process, confirming eligibility, reaching agreement in principle obtaining signed DSAs, receiving data sets, resolving data queries, and reformatting study data sets was extremely time-consuming and took much longer than the project team had anticipated. Problems encountered included difficulties in identifying contact addresses for authors (especially for papers published

before the internet era, where e-mails were not available, and institutional affiliations often vague), authors who did not reply to repeated e-mails and telephone messages, time taken to engage institutional legal teams in approving the DSA, and the fact that many legal teams wished to rewrite the template DSA provided, entailing much to and fro of drafts, and delay in resolving data queries with primary study authors. None of this was made easier by the fact that much of this data collection took place during the COVID-19 pandemic.

Our RoB assessment showed that for our primary outcome, repetition of self-harm, only six studies were rated as low RoB, with eight rated as high risk. The two main reasons for RoB concerns were collection of outcomes via self-report from non-blinded participants (Domain 4) and trials not having a pre-specified, published, analysis plan (Domain 5). Studies with a higher RoB in Domains 1 and 2 (randomisation processes and deviations from intended interventions) tended to be from earlier studies and/or pilot studies.

On our primary outcome, we found no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control for reducing repeat self-harm between randomisation and 3, 6, 12, 18, 24 or > 24 months. We observed promising effects for DBT at 6 months in our IPD + AD meta-analysis, but there was insufficient evidence to detect a statistically significant reduction in self-harm compared to control, and this trend was not seen in our IPD analysis or at other time points.

We observed high levels of within-study variability in outcomes, and generally low between-study heterogeneity in treatment effects, except for a few studies of CAT/MBT at 3 months, GT at 12 months and CBT at 18 months. We found no evidence for differential treatment effects according to study- and treatment-level candidate moderators, small study effects or publication bias, and sensitivity analyses led to no changes to our conclusions.

For secondary outcomes, we also found no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control on time to repetition of self-harm, pattern of self-harm repetition (within 6-month periods post randomisation), or depression at any time point. However, there was good evidence that interventions overall had a small positive effect on general psychopathology at 12 months in IPD and IPD + AD meta-analysis. There was no further evidence for any therapeutic intervention overall at other time points, but was some limited evidence from single studies in support

of CBT, DBT and PST at certain time points using IPD (not supported for DBT when including additional AD).

There was good evidence that interventions overall had a small positive effect on suicidal ideation at 6 months in IPD + AD meta-analysis, but insufficient evidence for specific interventions (with only two to four studies available per intervention).

In our exploratory IPD meta-analysis of the moderating effect of a range of individual participant characteristics on the treatment effect, we observed a notable improvement in treatment effect for participants with multiple previous self-harm episodes, compared with those with fewer episodes on repetition of self-harm 6–12 months post randomisation, accompanied by a consistent trend across other outcomes. Overall, we also noted a slight trend towards better treatment outcomes among older participants, across most outcomes, most notably in CBT and PST.

We further observed trends suggesting potential differential treatment effects linked to participants' age, gender, self-harm method, and anxiety and some evidence suggesting an enhanced treatment effect for males compared with females in managing depression, as indicated by unadjusted CIs at both 6 and 12 months. There was a slight overall trend towards better treatment outcomes for participants who presented with self-poisoning rather than self-injury, particularly in terms of repetition of self-harm and suicidal ideation, most notably at 6 and 12 months, respectively.

Strengths

Our search strategy was a strength, in that we utilised a detailed two-step approach enabling a rigorous identification of RCTs. In the first step, we harvested RCTs from existing systematic reviews. In our second step, we then conducted supplementary searches for recent or unpublished RCTs to fill gaps from the first search. Of the final 39 eligible studies, 30 were found from step 1 and 9 from step 2, the RCT update and 'gap-filling' searches. We developed pre-specified and rigorous inclusion criteria, and we also included trial registrations in the search. We believe these steps allowed us to minimise selection and publication bias.

We tried to ensure our included studies were as representative of clinical populations as possible by specifying in our inclusion criteria that trial participants had to have self-harmed prior to inclusion. Having identified potential studies, all records were then screened independently by two authors with a third adjudicating if

agreement could not be reached enhancing the credibility and trustworthiness of findings.

A second major strength is the IPD approach we adopted, enabling a comprehensive analysis across many studies, outcomes and moderators. IPD meta-analysis provides more robust estimates of the effects of therapeutic interventions for self-harm than conventional meta-analyses that rely on aggregated information and reported analyses,¹³ and significantly enhances the power to detect interaction effects. This study is the first of its kind to explore the crucial clinical problem of adolescent self-harm using IPD meta-analytic methods.

The IPD approach also allowed us to include studies where only a part of the sample was eligible. We were thus able to identify an additional 21 studies on top of the 18 studies with full sample eligibility. From these partial sample eligibility studies, we were able to include an extra 1783 participants. For comparison purposes, the most recent Cochrane review,⁹ using standard meta-analyses, included 17 trials with a total of 2280 participants compared with our final analysis set of 26 studies with 3448 eligible participants. This increase in studies and participants resulted in narrowed CIs and increased precision and gives more confidence in our findings.

Other important strengths include the wide geographical spread of studies and the range of interventions evaluated which differed in therapeutic orientation, intensity and duration. Some of the partial sample eligible studies enabled us to include interventions such as 'postcards' that had not been included in previous reviews.

We adopted a rigorous approach to our RoB ratings, using the well-established Cochrane tool, with each study rated independently by two authors with a third adjudicating if agreement could not be reached. We also involved the primary study authors who had shared data in a collaborative group, and this group was able to comment on and contribute to the analysis plan and the interpretation of findings.

Limitations

We note several potentially significant limitations in our study. Perhaps foremost of these is missing IPD. In some older studies, IPD were no longer available, but some authors of more recent primary studies felt unable to share their data. This was because of concerns that original ethical approval did not allow sharing, or that individual study participants might be identified. We offered the possibility of sharing only limited data sets to reduce the

likelihood (we thought always very low) of identification, but this was not acceptable.

For the full sample eligible studies, we were able to include the published data in our secondary IPD plus aggregate meta-analysis, but this was not possible for the partial sample eligible studies, or for meta-analysis of potential individual participant moderators. Two important full sample eligible studies regularly cited in systematic reviews as showing effectiveness of DBT in reducing self-harm did not share their data.^{56,69} Our IPD meta-analysis therefore includes only two small studies of DBT.^{35,64,65} We did include published data from these studies in our secondary IPD plus aggregate meta-analysis, and it should be noted that this did not lead to any changes in our conclusions. These studies were not rated as low RoB.

We were somewhat surprised at how few studies we identified in the literature, given the importance of self-harm. Also of note was the wide range of interventions evaluated, meaning that for any one intervention there were few good-quality studies and for some intervention types very few, with some subgroup analysis of only a single study. There was a lack of replication of findings, and on the one occasion when this occurred, Hazell *et al.*'s⁵⁰ replication of Wood *et al.*,⁶⁸ resulted in the earlier findings being contradicted.

We made some choices that might also be considered to have some limiting effects. We selected an age range of 11–18 years of age, determined largely by the cut points used in other large reviews. This will have had some implications for interpreting our results in regions where different age cut points for services apply.

Our choice of a binary primary outcome of any repetition of self-harm could also be seen as a limitation. We made this choice because of serious difficulties in accuracy and consistency of alternative measurements such as the number/frequency of self-harm across studies, particularly for those who self-harm repeatedly. Thus, our primary outcome described whether young people had self-harmed or not within 12 months post randomisation, not a reduction in the number of self-harm attempts, and our conclusions need to be understood in this light. Evidence from those with lived experience of NSSI suggest that recovery needs to be understood in more complex ways than just cessation or reduced frequency of self-harming behaviour.⁷⁰

Wider issues

A significant constraint was the time needed to obtain formal DSAs, effect the transfer of data and check data integrity, as well as ensure data received aligned with

already published results. Although clinical investigators were nearly always supportive, institutions usually had to be involved in signing off DSAs. Completing these important administrative steps took considerably longer than originally anticipated. Similar issues have been reported by others.⁷¹

Another significant limitation is the variability in the definitions and timings of outcomes, and measures used for data collection across the studies. This impacted on study heterogeneity and limited the ability to meaningfully pool studies and interpret pooled treatment effects. We defined multiple follow-up time points allowing us to pool treatment effects over consistent periods of time across the different studies. However, this resulted in multiple analyses each of fewer studies. Data collection methods also varied considerably. Some studies extracting data from medical records, some used clinical interview, some self- or parent-report. Often, combinations of these were used. When formal questionnaires were used, there was little consistency, with up to eight different measures used to collect data on a single construct, for example, depression.

When it came to exploring potential individual participant moderators, there was also a wide range of available data, with little consistency across studies. Gender and age were the only moderators consistently available across all studies. Other baseline characteristics such as family dysfunction, psychotropic medication, LGBTQ status, ASD, abuse, eating disorders, intellectual disability, looked after children and physical health problems were inconsistently collected, with < 50% of studies including these important characteristics. Most participants within studies were female, limiting the precision of estimates for the moderating effect of gender on repetition of self-harm. Even when age data were collected, the varying age ranges, perhaps reflecting different patterns of care in the locations where studies were conducted, limited the interpretation of the moderating effect of age.

From an analytic perspective, it should be noted that when fewer than 10 trials are included in the meta-analysis, when trials are small, or when the outcome is rare, no currently available method can reliably estimate the heterogeneity.²⁷ The inconsistency in moderator data collected, and the ways in which it was collected in the primary studies, further limited the number of studies included in each analysis, particularly in analysis by intervention. Where possible, we used standardisation of effects within each study and by time point to account for this. But different derivations and definitions of moderators within each study were required depending on eligibility and data collection. More sophisticated analysis approaches were

considered to account for some of the data complexities (see [Report Supplementary Material 1](#)), but it was felt that while none would alter the conclusions materially, they would add to the complexity of conducting and reporting the analyses. These are left for future research.

Conclusions and implications

Our findings are broadly similar to those of Cochrane, but the IPD approach brings a strong reinforcement of these findings from an analysis with substantially more studies and participants. This increased confidence and precision is clinically important. We need to stress that, in line with the recent Cochrane review,⁹ we found no evidence that interventions were more or less effective than control treatments. We did not find that treatments were ineffective.

We believe our findings also act as a counterweight to the conclusions of some relatively small (underpowered) evaluations of the long-term effectiveness of psychological therapies in treating self-harm in adolescents. We disagree with Kothgassner¹⁰ that, overall, any intervention is more effective than active controls. We also disagree with some of the recommendations of the most recent NICE guideline¹² and conclude that more caution may be needed when considering the effectiveness of DBT. The NICE findings noted that there was no evidence of the effect of DBT-A on repeat self-harm by 12-month follow-up, with positive findings only at 6 months, just after the cessation of a very intensive intervention. These results align most closely with our 6-month time point findings and explain (along with some differences in the statistical methods for all outcomes due to more robust allowance for uncertainty in the heterogeneity) our different conclusions.

Despite the public health importance of self-harm, its many adverse outcomes, and a rigorous IPD meta-analysis design, we therefore cannot recommend a specific, safe intervention to prevent repetition among those who present with self-harm.

We hypothesise a number of reasons why this might be the case. Despite a recent increase in well-conducted studies, we were only able to pool a relatively small number of studies, once different interventions, end points and follow-up times were considered. Nearly all the studies we examined looked at specific, manualised, interventions compared with a control treatment – usually TAU or ‘enhanced treatment as usual’. It may be that experienced practitioners delivering control treatments were able to conduct personalised assessments and tailor their interventions to individual needs, unlike therapists in the intervention arms of trials who were constrained to

deliver a less-flexible, manualised treatment. If this were the case, it is plausible that both interventions might be effective, reducing observed effect sizes.

Finally, our findings might reflect the nature of the standardised interventions evaluated, which focus to a large degree on risk assessment and management. This nearly always includes encouragement to report self-harm, which may inflate incidence of reported repeat self-harm in the follow-up period. Some support for this argument comes from our findings that there were generally more positive (but not significant) effects across studies for general psychopathology, depression and suicidal ideation, compared to self-harm outcomes.

Our findings related to individual participant moderators are also unable to generate definitive clinical recommendations. However, we observed some evidence for improvement in treatment effect for participants with multiple previous self-harm episodes, compared with those with fewer episodes on repetition of self-harm 6–12 months post randomisation, with a consistent trend across other outcomes. We also noted a slight trend towards better treatment outcomes among older participants, across most outcomes, most notably in CBT and PST. There was a slight overall trend towards better treatment outcomes for participants who presented with self-poisoning rather than self-injury, particularly in terms of repetition of self-harm and suicidal ideation, most notably at 6 and 12 months, respectively.

It is important to emphasise that young people who self-harm are at elevated risk for many adverse outcomes and should undoubtedly receive help and support. Our findings indicate that those who have engaged in recurrent self-harm (defined here as more than two previous episodes) might respond more positively to treatment. Given their higher risk, it is imperative that they are thoroughly assessed and offered an intervention deemed most appropriate by a trained and qualified clinician.

Research recommendations

Individual participant data meta-analyses are likely to remain a rich source of understanding of the literature, and the best way of drawing conclusions from multiple individual studies in the future. In this first such analysis of self-harm in adolescents, we have shown that it is possible to conduct such a study but that it is very time-consuming despite clear guidance from funding bodies that researchers should share data appropriately.^{72,73} We are not alone in drawing this conclusion.⁷¹ To facilitate future data-sharing, more attention needs to be paid to seeking appropriate consent from study participants for (pseudo) anonymised data-sharing. Institutions generally

need to collaborate on template DSAs, and researchers need to adopt Open Science principles in self-harm research.⁷⁴ The lack of availability of data that are currently being used in informing treatment guidelines is a concern.

We need innovative ideas about optimising standard care and alternative interventions (perhaps rooted more carefully in theoretical considerations or mechanisms that drive self-harm) and collaborative research programmes to rapidly execute large-scale, well-designed studies. Studies should also include better descriptions of comparator treatments and routine monitoring and reporting of treatment integrity.

Few studies were rated as low RoB, although this is likely to change as researchers start to publish pre-specified analysis plans as a matter of routine. This suggests that researchers and funders need to focus more carefully on research design. However, traditional RCT designs may not be the most effective way forward. We suggest more consideration of efficient platform trial designs,⁷⁵ evaluating multiple treatments under a single protocol, allowing for modifications to the trial design in response to interim results, or factorial trial designs that focus on optimising fixed or adaptive interventions. Such approaches are better suited to address multiple research questions and to determine the most effective interventions for different individuals, while simultaneously ensuring consistency in research methods.

Development and agreement of core outcome sets for self-harm trials is vital and would increase the homogeneity of outcome reporting, allowing future studies to be pooled more efficiently and inclusively.⁷⁶ A clear and agreed definition of the primary outcome with agreed times for follow-up is critical, but we also need agreement and consensus on the moderators to be included in future studies. Many moderators deemed important are currently barely collected. Ensuring that these are consistently included in future research will greatly enhance the quality and applicability of the findings. More systematic data on health economic outcomes would also be valuable. To develop such an outcome set may require an international conference or series of meetings for the scientific and service user communities.

Additional information

CRedit contribution statement

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Data-sharing statement

The data from the individual studies in this report were obtained under formal data-sharing agreements which do not allow further sharing of the data. Any queries should be submitted to the corresponding author.

Ethics statement

Formal ethical approval for the project was provided on 5 July 2019 by the University of Leeds, Faculty of Medicine and Health Ethics Committee – MREC 18-098.

Information governance statement

The project was sponsored by the University of Leeds (Grant Number: RG.PSRY.116370). An independent Study Steering Group including independent clinical and statistical experts with relevant expertise and a PPI representative provided independent oversight of the project.

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Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at <https://doi.org/10.3310/KKBB1164>.

Primary conflicts of interest: David Cottrell: at the time the award that funded this research was granted, was Co-Chair of the NIHR Advanced Fellowship Panel. Chair of TSC BeST? (NIHR PHR 12/211/54) and of IVY DMEC (NIHR127408).

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Amanda Farrin: was member of the NIHR funding committee (HTA Clinical Trials and Evaluation until November 2018), the NIHR CTU Standing Advisory Committee, and is an NIHR Senior Investigator. She has received grants from NIHR (Infrastructure and methodological funding: NIHR155210 and NIHR135115; HTA: NIHR156616 and NIHR131334 and 17/33/03 and 17/33/03 and 16/162/01 and 15/130/11 and 15/43/07; HS&DR: NIHR151848 and NIHR132197 and 16/04/13 and 16/04/06; PGfAR: RP-DG-0218-10001 and RP-PG-0617-20001 and RP-PG-1016-20005 and RP-PG-1016-20007 and RP-PG-0216-20003 and RP-PG-0615-20019 and RP-PG-0514-20009; EME: 15/74/01; MRC/NIHR: TMRP/WG/15 and HRB-TMRN-2017-1).

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Faraz Mughal: NIHR Doctoral Fellowship NIHR300957, Chair of DMEC NIHR ASSURED programme RP-PG-0617-20004, Member SSC CASCADE study NIHR RfPB NIHR203506 and Co-lead of NIHR School for Public Health Research PHRESH consortium Public Mental Health Theme. Member of the current NICE self-harm clinical guideline development committee.

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This synopsis was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Publications

Wright-Hughes A, Walwyn R, Farrin AJ and Cottrell. *Accounting for Treatment Heterogeneity in Systematic Reviews of Trials of Complex Interventions*. Conference paper at International Clinical Trials Methodology Conference, 2019.

Wright-Hughes A, Walwyn R, Wright J, Farrin A, Fonagy P, Ougrin D, *et al*. Reducing self-harm in adolescents. An individual participant data meta-analysis (RISA-IPD): systematic review protocol. *BMJ Open* 2021;**11**:e049255.

Cottrell D, Wright-Hughes A, Farrin A, Walwyn R, Mughal F, Truscott A. Reducing self-harm in adolescents: the RISA-IPD individual patient data meta-analysis and systematic review. *Health Technol Assess* 2024. <https://doi.org/10.3310/GTNT6331>

Wright-Hughes A, Farrin AJ, Fonagy P, Ougrin D, Stahl D, Wright J, *et al.* Systematic review and individual participant data meta-analysis: reducing self-harm in adolescents: Pooled treatment effects, study, treatment and participant moderators. *J Am Acad Child Adolesc Psychiatry* 2025. <https://doi.org/10.1016/j.jaac.2025.01.017>.

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List of abbreviations

AD	aggregate data
BPD	borderline personality disorder
CAT	cognitive analytic therapy
CBT	cognitive-behavioural therapy
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval (in pooled analysis the HKSJ adjusted confidence for uncertainty in variance estimate is presented)
CI*	confidence interval (without HKSJ adjustment in pooled analysis)
CTRU	Clinical Trials Research Unit
DBT	dialectical behaviour therapy
DSA	data-sharing agreement
FT	family therapy
GT	group therapy
HKSJ	Hartung-Knapp-Sidik-Jonkman
IPD	individual participant data
ITT	intention to treat
MA	meta-analysis
MBT	Mentalisation-Based Therapy
MeSH	medical subject heading
MST	multisystemic therapy
NICE	National Institute for Health and Care Excellence
NSSI	non-suicidal self-injury
PPIE	patient and public involvement and engagement
PRESS	Peer Review of Electronic Search Strategies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PST	problem-solving, psychoeducation, support
RCT	randomised controlled trial
REML	restricted maximum likelihood
RoB	risk of bias

SAP	statistical analysis plan
SMD	standardised mean difference
SUAG	Service User Advisory Group
TAU	treatment as usual

List of supplementary material

Report Supplementary Material 1

Full statistical analysis plan

Report Supplementary Material 2

Invitation to primary authors to collaborate

Report Supplementary Material 3

Template data sharing agreement, including data requested

Report Supplementary Material 4

Results of individual studies (step 1) and meta-analysis forest plots (step 2)

Supplementary material can be found on the NIHR Journals Library report page (<https://doi.org/10.3310/KKBB1164>).

Supplementary material has been provided by the authors to support the report, and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

The supplementary materials (which include but are not limited to related publications, patient information leaflets and questionnaires) are provided to support and contextualise the publication. Every effort has been made to obtain the necessary permissions for reproduction, to credit original sources appropriately, and to respect copyright requirements. However, despite our diligence, we acknowledge the possibility of unintentional omissions or errors and we welcome notifications of any concerns regarding copyright or permissions.

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Appendix 1 Search 1 search strategies to identify systematic reviews

Introduction

The search strategies listed here were used to identify systematic reviews of interventions for self-harm in adolescents.

Information resources searched

Cochrane Database of Systematic Reviews (Wiley) Issue 6 of 12, June 2019

EMBASE Classic + EMBASE (Ovid) 1947–20 June 2019

Epistemonikos <https://epistemonikos.org/>

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946–20 June 2019

PROSPERO <https://crd.york.ac.uk/prospero/>

PsycInfo (Ovid) 1806–Week 2, June 2019

Search strategies

Cochrane Database of Systematic Reviews Issue 6 of 12, June 2019

Date searched: 6 June 2019

Records found: Eight

IDSearchHits

- #1 MeSH descriptor: [Self-Injurious Behavior] this term only 271
- #2 MeSH descriptor: [Suicide] this term only 601
- #3 MeSH descriptor: [Suicide, Attempted] this term only 360
- #4 MeSH descriptor: [Drug Overdose] this term only 127
- #5 MeSH descriptor: [Self Mutilation] this term only 33
- #6 (selfharm* or selfinjur* or selfinflict* or "self harm*" or "self injur*" or "self inflict*"):ti 284
- #7 ((self or themsel* or onesel*) near/2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)):ti 379
- #8 (auto near/2 (aggress* or mutilat*)):ti 4
- #9 (automutilat* or "auto mutilation*" or autoaggress* or "auto agress*"):ti 4
- #10 suicid*:ti 1481

- #11 (parasuicid* or para-suicid*):ti 31
- #12 ((deliberat* or intentional or intended) near/2 (overdos* or poison* or self poison*)):ti 79
- #14 (overdos* or poison):ti 222
- #15 NSSI:ti 0
- #16 (headbang* or head-bang*):ti 0
- #17 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 2423
- #18 MeSH descriptor: [Adolescent] this term only 99786
- #19 (teenage* or adolescen* or youth) 134000
- #20 MeSH descriptor: [Young Adult] this term only 218
- #21 (young* adj (people* or person* or adult* or m?n or wom?n)) 1132
- #22 MeSH descriptor: [Child] this term only 1093
- #23 (school* adj2 (pupil* or student*)):tw. 9485
- #24 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj (yr? or year?)):tw. 9484
- #25 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)) 354
- #26 (teen or teens or juvenil*) 4791
- #27 #18 or #19 or #20 or #21 or #22 or #23 or #24 or #26 143881
- #28 #17 and #2 7730

Limit to Cochrane Database of Systematic Reviews 8

EMBASE Classic + EMBASE (Ovid) 1947–20 June 2019

Date searched: 21 June 2019

Records found: 322

-
- 1 *automutilation/ (7762)
 - 2 *suicide/ or *suicide, attempt/ (40508)
 - 3 *Drug Overdose/ (9293)
 - 4 (selfharm* or selfinjur* or selfinflict* or "self harm*" or "self injur*" or "self inflict*"):ti. (5763)
 - 5 ((self or themsel* or onesel*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)):ti. (8760)
 - 6 (auto adj (aggress* or mutilat*)):ti. (75)
 - 7 (automutilat* or "auto mutilation*" or autoaggress* or "auto agress*"):ti. (292)
 - 8 suicid*.ti. (48944)
 - 9 (parasuicid* or para-suicid*):ti. (418)
 - 10 ((deliberat* or intentional or intended) adj2 (overdos* or poison* or self poison*)):ti. (535)
 - 11 (poison adj2 (deliberat* or intentional or intended)):ti. (4)
 - 12 (overdos* adj2 (deliberat* or intentional or intended)):ti. (191)

- 13 NSSI.ti. (56)
- 14 (headbang* or head-bang*).ti. (86)
- 15 or/1-14 (74633)
- 16 Adolescent/ (1577703)
- 17 (teenage* or adolescen* or youth).tw. (406857)
- 18 young adult/ (295046)
- 19 (young* adj (people* or person* or adult* or m?n or wom?n)).tw. (240389)
- 20 child/ (1862127)
- 21 (school* adj2 (pupil* or student*)).tw. (25707)
- 22 (teen or teens or juvenil*).tw. (113717)
- 23 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)).tw. (989096)
- 24 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj (yr? or year?)).tw. (750109)
- 25 or/16-24 [Adolescents] (3888109)
- 26 15 and 25 (20956)
- 27 ((systematic adj2 review* or meta-analys* or "meta analysis" or "meta-regression" or "meta regression"). ti. (199945)
- 28 limit 26 to (meta analysis or "systematic review") (276)
- 29 26 and 27 (189)
- 30 28 or 29 [SRs + Self Harm + Adolescents] (322)

Epistemonikos <https://epistemonikos.org/>

Date searched: 6 June 2019

Records found: 392

(advanced_title_en:(advanced_title_en:(advanced_title_en:(advanced_title_en:(Self-Injurious Behavior)) OR advanced_title_en:(suicid*) OR advanced_title_en:(Drug Overdose) OR advanced_title_en:(selfharm* OR selfinjur* OR selfinflict* OR "self harm*" OR "self injur*" OR "self inflict*").) OR advanced_title_en:(self OR themsel* OR onesel*) AND (aggress* OR harm* OR cutt* OR immolat* OR inflict* OR injur* OR mutilat* OR poison* OR damag* OR destruct*))) OR advanced_title_en:(automutilat* OR "auto mutilation*" OR autoaggress* OR "auto agres*")) OR advanced_title_en:(parasuicid* OR para-suicid*) OR advanced_title_en:(deliberat* OR intentional OR intended) AND (overdos* OR poison* OR self poison*)) OR advanced_title_en:(poison AND (deliberat* OR intentional OR intended)) OR advanced_title_en:(overdos* AND (deliberat* OR intentional OR intended)).) OR advanced_title_en:(NSSI) OR advanced_title_en:(headbang* OR head-bang*)) OR advanced_abstract_en:(advanced_title_en:(advanced_title_en:(advanced_title_en:(Self-Injurious Behavior)) OR advanced_title_en:(suicid*) OR advanced_title_en:(Drug Overdose) OR advanced_title_en:(selfharm* OR selfinjur* OR selfinflict* OR "self harm*"

OR "self injur*" OR "self inflict*").) OR advanced_title_en:(self OR themsel* OR onesel*) AND (aggress* OR harm* OR cutt* OR immolat* OR inflict* OR injur* OR mutilat* OR poison* OR damag* OR destruct*))) OR advanced_title_en:(automutilat* OR "auto mutilation*" OR autoaggress* OR "auto agres*")) OR advanced_title_en:(parasuicid* OR para-suicid*) OR advanced_title_en:(deliberat* OR intentional OR intended) AND (overdos* OR poison* OR self poison*)) OR advanced_title_en:(poison AND (deliberat* OR intentional OR intended)) OR advanced_title_en:(overdos* AND (deliberat* OR intentional OR intended)).) OR advanced_title_en:(NSSI) OR advanced_title_en:(headbang* OR head-bang*)) AND (advanced_title_en:(teenage* OR adolescen* OR youth OR young OR pupil OR student OR schoolchild OR child OR teen* OR juvenil*) OR ("11" OR "12" OR "13" OR "14" OR "15" OR "16" OR "17" OR "18" OR "19") AND (year? OR yr? OR old OR age?)).) OR advanced_abstract_en:(teenage* OR adolescen* OR youth OR young OR pupil OR student OR schoolchild OR child OR teen* OR juvenil*) OR ("11" OR "12" OR "13" OR "14" OR "15" OR "16" OR "17" OR "18" OR "19") AND (year? OR yr? OR old OR age?)).) [Filters: classification=systematic-review, protocol=no] 392

Ovid MEDLINE(R) and Epub ahead of print, in-process & other non-indexed citations and daily 1946–20 June 201

Date searched: 21 June 2019

Records found: 346

-
- 1 Self-Injurious Behavior/ (7200)
 - 2 suicide/ or suicide, attempted/ (51983)
 - 3 Drug Overdose/ (10369)
 - 4 Self Mutilation/ (3180)
 - 5 (selfharm* or selfinjur* or selfinflict* or "self harm*" or "self injur*" or "self inflict*").ti. (4978)
 - 6 ((self or themsel* or onesel*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)).ti. (7491)
 - 7 (auto adj (aggress* or mutilat*)).ti. (75)
 - 8 (automutilat* or "auto mutilation*" or autoaggress* or "auto agres*").ti. (222)
 - 9 suicid*.ti. (40905)
 - 10 (parasuicid* or para-suicid*).ti. (332)
 - 11 ((deliberat* or intentional or intended) adj2 (overdos* or poison* or self poison*)).ti. (413)
 - 12 (poison adj2 (deliberat* or intentional or intended)).ti. (3)
 - 13 (overdos* adj2 (deliberat* or intentional or intended)).ti. (138)

- 14 NSSI.ti. (52)
 15 (headbang* or head-bang*).ti. (70)
 16 or/1-15 (80097)
 17 Adolescent/ (1939543)
 18 (teenage* or adolescen* or youth).tw. (304577)
 19 young adult/ (749895)
 20 (young* adj (people* or person* or adult* or m?n or wom?n)).tw. (173989)
 21 child/ (1620458)
 22 (school* adj2 (pupil* or student*)).tw. (20810)
 23 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj (yr? or year?)).tw. (471642)
 24 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)).tw. (618630)
 25 (teen or teens or juvenil*).tw. (87194)
 26 or/17-25 (3594742)
 27 and/16,26 (28777)
 28 ((systematic adj2 review*) or meta-analys* or "meta analysis" or "meta-regression" or "meta regression").ti. (162612)
 29 limit 27 to (meta analysis or "systematic review") (290)
 30 27 and 28 (271)
 31 29 or 30 [srs + self harm+ adolescents] (346)

PROSPERO <https://crd.york.ac.uk/prospero/>

Date searched: 06 June 2019

Records found: 123

- #1 MeSH DESCRIPTOR Suicide, Attempted
 #2 MeSH DESCRIPTOR Suicide 190
 #3 MeSH DESCRIPTOR Self-Injurious Behavior 91
 #4 MeSH DESCRIPTOR Self Mutilation 0
 #5 selfharm* or selfinjur* or selfinflict* or "self harm*" or "self injur*" or "self inflict*":TI 72
 #6 ((self or themsel* or onesel*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)): TI 78
 #7 (auto adj (aggress* or mutilat*)):TI 0
 #8 suicid* or parasuicid* or para-suicid*:TI 256
 #9 (automutilat* or "auto mutilation*" or autoaggress* or "auto agres*"):TI 6
 #10 overdos* or poison*:TI 44
 #11 NSSI3
 #12 headbang* or head-bang* 0
 #13 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 356
 #14 MeSH DESCRIPTOR Adolescent 1686
 #15 MeSH DESCRIPTOR Young adult 195
 #16 MeSH DESCRIPTOR Child 3884

- #17 teenage* or adolescen* or youth or young or teen or teens or juvenil* 7962
 #18 (school* adj2 (pupil* or student*)) 1424
 #19 #14 OR #15 OR #16 OR #17 OR #18 15151
 #20 #15 AND #21 123

PsycInfo (Ovid) 1806-Week 2, June 2019

Date searched: 21 June 2019

Records found: 164

- 1 *Self-Injurious Behavior/ (3109)
 2 *suicide/ or ATTEMPTED SUICIDE/ (29252)
 3 *Drug Overdoses/ (1341)
 4 *Self-Mutilation/ (1006)
 5 (selfharm* or selfinjur* or selfinflict* or "self harm*" or "self injur*" or "self inflict*").ti. (4830)
 6 ((self or themsel* or onesel*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)).ti. (6406)
 7 (auto adj (aggress* or mutilat*)).ti. (18)
 8 (automutilat* or "auto mutilation*" or autoaggress* or "auto agres*").ti. (30)
 9 suicid*.ti. (33008)
 10 (parasuicid* or para-suicid*).ti. (346)
 11 ((deliberat* or intentional or intended) adj2 (overdos* or poison* or self poison*)).ti. (114)
 12 (poison adj2 (deliberat* or intentional or intended)).ti. (3)
 13 (overdos* adj2 (deliberat* or intentional or intended)).ti. (20)
 14 NSSI.ti. (65)
 15 (headbang* or head-bang*).ti. (43)
 16 or/1-15 (43517)
 17 (teenage* or adolescen* or youth).tw. (302025)
 18 (young* adj (people* or person* or adult* or m?n or wom?n)).tw. (94804)
 19 (school* adj2 (pupil* or student*)).tw. (68733)
 20 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj (yr? or year?)).tw. (154851)
 21 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)).tw. (271489)
 22 (teen or teens or juvenil*).tw. (36683)
 23 or/17-22 (647709)
 24 and/16,23 (13081)
 25 ((systematic adj2 review*) or meta-analys* or "meta analysis" or "meta-regression" or "meta regression").ti. (30089)

- 26 limit 24 to (meta analysis or “systematic review”) (164)
 27 24 and 26 (164)
 28 26 or 27 (164)

Appendix 2 Search 2 search strategies to identify randomised controlled trials

Introduction

The search strategies listed here were used to identify reports of RCTs of interventions for self-harm in adolescents.

We searched all information resources in 2019 and ran update searches on a limited set of databases in 2020 and 2021. Minor modifications were made to some search strategies between 2019 and 2021 which increased their sensitivity. These modifications are described in the main manuscript.

The most recent search strategy conducted in each information resource is reported.

Information resources searched

ClinicalTrials.gov <https://clinicaltrials.gov/>

Cochrane Central Register of Controlled Trials (Wiley) Issue 1 of 12, January 2022

Conference Proceedings Citation Index- Science (Web of Science) 1990+

Conference Proceedings Citation Index – Social Science & Humanities (Web of Science) 1990+

Dissertations & Theses A&I (ProQuest)

EMBASE Classic + EMBASE (Ovid) 1947–20 January 2022

Epistemonikos <https://epistemonikos.org/>

Europe PMC Grantfinder <https://europepmc.org/grantfinder>

Headspace National Youth Mental Health Foundation <https://headspace.org.au/>

International Clinical Trials Registry Platform <https://apps.who.int/trialsearch/>

Ovid MEDLINE(R) ALL 1946–20 January 2022

National Health and Medical Research Council (Australia) <https://nhmrc.gov.au/>

APA PsycInfo (Ovid) 1806–Week 3, January 2022

Search strategies

ClinicalTrials.gov <https://clinicaltrials.gov/>

Date searched: 13 August 2019

Records found: 165

self harm OR overdose OR “self inflict*” OR “self injur*” | Suicide, Attempted OR suicide OR self harm

Applied Filters: Child (birth–17)

Cochrane Central Register of Controlled Trials. (Wiley) Issue 1 of 12, January 2022

Date searched: 21 January 2022

Records found: 1308

IDSearch

- #1 MeSH descriptor: [Self-Injurious Behavior] this term only
- #2 MeSH descriptor: [Suicide] this term only
- #3 MeSH descriptor: [Suicide, Attempted] this term only
- #4 MeSH descriptor: [Suicide, Completed] this term only
- #5 MeSH descriptor: [Drug Overdose] this term only
- #6 MeSH descriptor: [Self Mutilation] this term only
- #7 (selfharm* or selfinjur* or selfinflict*):ti,ab,kw
- #8 ((self or themsel* or onesel*) near/2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)):ti,ab,kw
- #9 (autoaggress* or “auto aggress*” or auto-aggress):ti,ab,kw
- #10 (automutilat* or “auto mutilat*” or auto-mutilat*):ti,ab,kw
- #11 suicidality:ti,ab,kw
- #12 (parasuicid* or para-suicid*):ti,ab,kw
- #13 (suicid* near/2 (attempt* or behavio* or intent* or intend* or commit*)):ti,ab,kw
- #14 (suicid* near/2 (death or die* or morality or complete)):ti,ab,kw
- #15 ((deliberat* or intentional or intended) near/2 (overdos* or poison* or self poison*)):ti,ab,kw

#16 (poison near/2 (deliberat* or intention* or intend- ed)):ti,ab,kw
 #17 (overdos* or poison):ti,ab,kw
 #18 NSSI:ti,ab,kw
 #19 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #15 or #16 or #17 or #18
 #20 MeSH descriptor: [Adolescent] this term only
 #21 (teenage* or adolescen* or youth or child*): ti,ab,kw
 #22 MeSH descriptor: [Young Adult] this term only
 #23 (young* near/2 (people* or person* or adult* or m?n or wom?n)):ti,ab,kw
 #24 MeSH descriptor: [Child] this term only
 #25 (school* near/2 (pupil* or student*)):ti,ab,kw
 #26 (“11” or “12” or “13” or “14” or “15” or “16” or “17” or “18” or “19”) near/4 (old or age?):ti,ab,kw
 #27 (teen or teens or juvenil*):ti,ab,kw
 #28 #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27
 #29 #19 and #28 with Publication Year from 2015 to 2021, in Trials 1097 records

Conference Proceedings Citation Index – Science (Web of Science) 1990–present and Conference Proceedings Citation Index- Social Science & Humanities (Web of Science) 1990–present (searched simultaneously)

Date searched: 12 August 2019

Records found: 83

1283 #11 AND #10
 # 11712,424 TS= (clinical trial*) OR TS=(research design) OR TS= (comparative stud*) OR TS= (evaluation stud*) OR TS= (controlled trial*) OR TS= (follow-up stud*) OR TS= (prospective stud*) OR TS= (random*) OR TS= (placebo*) OR TS= (single blind*) OR TS= (double blind*)
 # 10646 #9 AND #8
 # 9 178,643 TS= (teenage* OR teen OR teens OR juvenil* OR adolescen* OR youth OR child*) OR TS= (school* adj2 (pupil* or student*))
 # 8 3,874#7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
 # 7 20 TS= (overdos* near/2 (deliberat* or intentional or intended))
 # 6 33 TS= (poison near/2 (deliberat* or intentional or intended))
 # 5 288TS= (suicid* near/2 (death or die* or morality or complete*))
 # 4 1,631TS= (suicid* near/2 (attempt* or behavio* or intent* or intend* or commit*))
 # 3 262TS= (suicid* near/2 (death or die* or morality or complete))

2 1,785TS=((self or themsel* or onesel*) near/2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*))
 # 1 1,161TS=(“Self-Injurious Behavio\$r” OR “Self Mutilation” OR suicidality OR “attempted suicide” OR self-harm* OR selfinjur* OR selfinfect* OR “self harm*” OR “self injur*” OR “self inflict*” OR autoaggress* OR “auto aggress*” or auto-aggress* OR automutilat* or “auto mutilat*” or auto-mutilat* OR NSSI)

Dissertations and Theses A&I (ProQuest) 1743–present

Date searched: 13 August 2019

Records found: 43

((ti(selfharm* OR selfinjur* OR selfinfect* OR (“self harm” OR “self harming”) OR (“self injuring” OR “self injurious” OR “self injury”) OR (“self inflicted”)) OR ti((self OR themsel* OR onesel*) NEAR/2 (aggress* OR harm* OR cutt* OR immolat* OR inflict* OR injur* OR mutilat* OR poison* OR damag* OR destruct*)) OR ti(auto NEAR/1 (aggress* ORmutilat*))OR ti(auto NEAR/1 (aggress* OR mutilat*))OR ti(automutilat* OR “auto mutilation*” OR autoaggress* OR “auto aggress*”) OR ti(suicide*) OR ti(parasuicid* OR parasuicide*) OR ti(deliberat* OR intentional OR intended NEAR/2 overdos* OR poison* OR self poison*) OR (poison NEAR/2 (deliberat* OR intentional OR intended)) OR ti((overdos* NEAR/2 (deliberat* OR intentional OR intended))) OR ti(overdos* NEAR/2 (deliberat* OR intentional OR intended))OR (overdos* NEAR/2 (deliberat* OR intentional OR intended)) OR ti(NSSI))) OR (su(Self-Injurious Behavio?r) OR su(drug overdose) OR su(suicide) OR su(attempted suicide) OR su(self mutilation)))

AND

(su(Adolescent) OR su(young adult) OR su(child) OR diskw((teenage* OR adolescen* OR youth OR child*)) OR diskw((young* NEAR/1 (people* OR person* OR adult* OR m?n OR wom?n))) OR diskw((school* NEAR/2 (pupil* OR student*))) OR diskw(teen OR teens OR juvenil*))

AND

(recurr* OR repeat* OR repetiti* OR re-occur* OR re occur* OR regress* OR history OR once OR twice OR episode*) AND noft(“clinical trial*” OR “controlled trial*” OR random* OR “single blind*” OR “double blind*” OR “research design” OR “comparative stud*” OR “evaluation stud*” OR “follow-up stud*” OR “prospective stud*”)

**EMBASE Classic + EMBASE (Ovid)
1947–20 January 2022**

Date searched: 21 January 2022

Records found: 603

1 automutilation/ (21466)
 2 suicide/ (65020)
 3 exp *Drug Overdose/ or *Opiate Overdose/(9984)
 4 *suicide attempt/ (13098)
 5 (selfharm* or selfinjur* or selfinflict*).tw,kw. (424)
 6 ((self or themself* or oneself*) adj2 (aggress* or
 harm* or cutt* or immolat* or inflict* or injur* or
 mutilat* or poison* or damag* or destruct*).tw,kw.
 (29538)
 7 (automutilat* or "auto mutilat*" or auto-
 mutilat*).tw,kw. (235)
 8 (autoaggress* or "auto aggress*" or auto-
 aggress).tw,kw. (1582)
 9 suicidality.tw,kw. (10333)
 10 (parasuicid* or para-suicid*).tw,kw. (937)
 11 (suicid* adj2 (death or die* or morality or complete)).
 tw,kw. (5095)
 12 (suicid* adj2 (attempt* or behavio* or intent* or
 intend* or commit*).tw,kw. (41385)
 13 (poison adj2 (deliberat* or intentional or intended)).
 tw,kw. (23)
 14 (overdos* adj2 (deliberat* or intentional or intend-
 ed)).tw,kw. (1094)
 15 NSSI.tw,kw. (1573)
 16 or/1-15 [Self harm or suicide] (137489)
 17 Adolescent/ (1783960)
 18 (teenage* or adolescen* or youth or child*).tw,kw.
 (2370688)
 19 young adult/ (441173)
 20 (young* adj (people* or person* or adult* or m?n or
 wom?n)).tw,kw. (288529)
 21 child/ (2161751)
 22 (school* adj2 (pupil* or student*).tw.
 (31569)
 23 (teen or teens or juvenil*).tw. (129776)
 24 (("11" or "12" or "13" or "14" or "15" or "16" or "17"
 or "18" or "19") adj4 (old or age?)).tw,kw.
 (1199060)
 25 high school student/ (8980)
 26 or/17-25 [Adolescents] (4900580)
 27 16 and 26 (45396)
 28 exp randomized controlled trial/
 (695793)
 29 exp double-blind procedure/ (194102)
 30 exp single-blind procedure/ (44931)

31 exp crossover-procedure/ (69529)
 32 ((singl* or doubl* or trebl* or tripl*) adj (blind* or
 mask*).tw. (264910)
 33 placebo/ (386669)
 34 placebo*.tw. (342596)
 35 randomization/ (93063)
 36 trial.ti. (356469)
 37 clinical trial*.tw. (612502)
 38 (randomly or randomis* or randomiz*).tw,kw.
 (1432485)
 39 controlled clinical trial/ (465155)
 40 or/28-39 [RCT or CCT] (2439340)
 41 exp animals/ not exp humans/ (5677771)
 42 exp nonhuman/ not exp human/
 (4918051)
 43 exp experimental animal/ (775489)
 44 exp veterinary medicine/ (60630)
 45 animal experiment/ (2770425)
 46 or/41-45 [Animal studies] (8163567)
 47 40 not 46 [Final RCT search] (2168486)
 48 27 and 47 (2757)
 49 limit 48 to yr="2018 -Current" (778)
 50 limit 49 to conference abstracts (175)
 51 49 not 50 (603)

Epistemonikos <https://epistemonikos.org/>

Date searched: 21 January 2022

Records found: 244

(title:(suicid* OR overdose OR selfharm* OR selfinjur*
 OR selfinflict* OR "self harm*" OR "self injur*" OR "self
 inflict*") OR abstract:(suicid* OR overdose OR selfharm*
 OR selfinjur* OR selfinflict* OR "self harm*" OR "self
 injur*" OR "self inflict*"))

AND

(title:(teenage* OR adolescen* OR youth OR child) OR
 abstract:(teenage* OR adolescen* OR youth OR child))

Limited by publication type to Primary Study

Limited by study design to RCT

Europe PMC Grantfinder

Date searched: 13 August 2019

Records found: 19

Suicide and child, Suicide and children, Suicide and
 adolescent, Suicide and adolescence

Self harm and child, Self harm and children, Self harm and adolescent, Self harm and adolescence

Self injury and child, self injury and children, self injury and adolescent, self injury and adolescence

Headspace research database <https://headspace.org.au/health-professionals/research-database/>

Date searched: 21-01-2022

Records found: 65

Searched research database by completing the filtered search as follows:

Mental health or substance use problem: Suicide & Self-Harm (any)

Stage of Illness: all

Treatment/Intervention: all

Publication date: 2015–all

Keyword: (left blank)

Advanced options: Randomized Controlled Trials selected

International Clinical Trials Registry Platform (WHO)
<https://apps.who.int/trialsearch/>

Date searched: 13 August 2019

Records found: 260 records for 211 trials

Title=suicide OR self-harm or self injur* or overdose

Condition=suicide OR self-harm or self injur* or overdose.
Search In Clinical trials in Children 2015-2019

Ovid MEDLINE(R) ALL <1946–10 February 2021>

Date searched: 21 January 2022

Records found: 556

Search Strategy:

- 1 Self-Injurious Behavior/ (8940)
- 2 suicide/ or suicide, attempted/ or Suicide, Completed/ (59340)
- 3 Drug Overdose/ (12975)
- 4 Self Mutilation/ (3229)
- 5 (selfharm* or selfinjur* or selfinflict*).tw,kw. (31)
- 6 ((self or themsel* or onesel*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*)).tw,kw. (22943)
- 7 (automutilat* or "auto mutilat*" or auto-mutilat*).tw,kw. (134)
- 8 (autoaggress* or "auto aggress*" or auto-aggress).tw,kw. (1024)
- 9 suicidality.tw,kw. (7687)
- 10 (suicid* adj2 (death or die* or morality or complete)).tw,kw. (4035)
- 11 (suicid* adj2 (attempt* or behavio* or intent* or intend* or commit*)).tw,kw. (30296)
- 12 (parasuicid* or para-suicid*).tw,kw. (667)
- 13 (poison adj2 (deliberat* or intentional or intended)).tw,kw. (15)
- 14 (overdos* adj2 (deliberat* or intentional or intend-ed)).tw,kw. (610)
- 15 NSSI.tw,kw. (1379)
- 16 or/1-15 [self harm] (104019)
- 17 Adolescent/ (2152902)
- 18 (teenage* or adolescen* or youth or child*).tw,kw. (1751741)
- 19 young adult/ (973874)
- 20 (young* adj (people* or person* or adult* or m?n or wom?n)).tw,kw. (209824)
- 21 child/ (1810341)
- 22 (school* adj2 (pupil* or student*)).tw,kw. (26573)
- 23 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)).tw,kw. (744797)
- 24 (teen or teens or juvenil*).tw,kw. (100553)
- 25 or/17-24 [adolescents] (4453304)
- 26 and/16,25 [self harm and adolescents] (41221)
- 27 randomized controlled trial.pt. (556317)
- 28 controlled clinical trial.pt. (94655)
- 29 randomized.ab. (547747)
- 30 placebo.ab. (224928)
- 31 clinical trials as topic.sh. (198920)
- 32 randomly.ab. (374356)
- 33 trial.ti. (255048)
- 34 27 or 28 or 29 or 30 or 31 or 32 or 33 (1421253)
- 35 exp animals/ not humans.sh. (4945885)
- 36 34 not 35 [Cochrane RCT precision maximising search filter] (1307487)
- 37 26 and 36 (2026)
- 38 limit 37 to yr="2018 -Current" (556)

National Health and Medical Research Council <https://nhmrc.gov.au/>

Date searched: 21 January 2022

Records found: 32 (screened and none downloaded)

Searched website for – suicide, 'self harm', 'self injury' (separate searches)

Browsed publications

APA PsycInfo <1806- Week 1, February 2021>

Date searched: 21 January 2022

Records found: 397

Search Strategy:

- 1 Self-Injurious Behavior/ (4924)
- 2 suicide/ or ATTEMPTED SUICIDE/ (36443)
- 3 Drug Overdoses/ (2264)
- 4 Self-Mutilation/ (1156)
- 5 head banging/ or self-inflicted wounds/ or self-poisoning/ (1158)
- 6 (selfharm* or selfinjur* or selfinfect*).tw,id. (52)
- 7 ((self or themself* or oneself*) adj2 (aggress* or harm* or cutt* or immolat* or inflict* or injur* or mutilat* or poison* or damag* or destruct*).tw,id. (22100)
- 8 (automutilat* or "auto mutilat*" or auto-mutilat*).tw,id. (48)
- 9 (autoaggress* or "auto aggress*" or auto-aggress).tw,id. (188)
- 10 suicidality.tw,id. (8395)
- 11 (parasuicid* or para-suicid*).tw,id. (775)
- 12 (suicid* adj2 (attempt* or behavio* or intent* or intend* or commit*).tw,id. (29356)

- 13 (suicid* adj2 (death or die* or morality or complete).tw,id. (3486)
- 14 (poison adj2 (deliberat* or intentional or intended).tw,id. (6)
- 15 (overdos* adj2 (deliberat* or intentional or intended).tw,id. (117)
- 16 NSSI.tw,id. (1668)
- 17 or/1-16 (68651)
- 18 (teenage* or adolescen* or youth or child*).tw,id. (953530)
- 19 (young* adj (people* or person* or adult* or m?n or wom?n)).tw,id. (112383)
- 20 (school* adj2 (pupil* or student*).tw,id. (75619)
- 21 (("11" or "12" or "13" or "14" or "15" or "16" or "17" or "18" or "19") adj4 (old or age?)).tw,id. (300758)
- 22 (teen or teens or juvenil*).tw,id. (40159)
- 23 or/18-22 (1205845)
- 24 and/17,23 (24744)
- 25 exp clinical trials/ or experimental design/ (24819)
- 26 exp treatment effectiveness evaluation/ (26970)
- 27 exp mental health program evaluation/ (2253)
- 28 exp random sampling/ (910)
- 29 randomi*.tw. (98224)
- 30 (clinic* adj4 trial*).tw. (41513)
- 31 (random* adj5 (assign* or allocat* or assort*).tw. (48723)
- 32 (crossover or cross-over).tw. (11165)
- 33 ((singl* or doubl* or tripl* or trebl*) adj (blind* or mask*).tw. (27755)
- 34 exp placebo/ (6166)
- 35 placebo*.tw. (42695)
- 36 or/25-35 [Trials] (216603)
- 37 24 and 36 (1008)
- 38 limit 37 to yr="2015 -Current" (397)

Appendix 3 Unconfirmed and ongoing studies

Study	Sample size/eligibility	Reference
<i>Unconfirmed-unable to contact author/s</i>		
Hurtado-Santiago 2018	N = 40, potentially partially eligible based on participants age (age 15–30)	<i>Effectiveness of the Iconic Therapy for Borderline Personality Disorder Symptoms</i> https://clinicaltrials.gov/show/nct03011190 Since published: Hurtado-Santiago S, Guzmán-Parra J, Bersabé RM, Mayoral F. Effectiveness of iconic therapy for the reduction of borderline personality disorder symptoms among suicidal youth: study protocol for a randomised controlled trial. <i>BMC Psychiatry</i> 2018 Dec; 18 :1. Hurtado-Santiago S, Guzmán-Parra J, Mayoral F, Bersabé RM. Iconic Therapy for the reduction of borderline personality disorder symptoms among suicidal youth: a preliminary study. <i>BMC Psychiatry</i> 2022 Dec; 22 :1.

Study	Sample size/eligibility	Reference
University 2015	N = 46 participants, potentially partially eligible based on prior self-harm and participants age (age 16 +)	<i>Treatment for Latino/a Adolescents with Suicidal Behavior</i> https://clinicaltrials.gov/ct2/show/NCT02820636
Dubois 1999	N = 102 participants, potentially partially eligible based on participant age (age 15–34)	Dubois L, Walter M, Bleton L. Évaluation comparative et prospective d'un protocole de prise en charge spécifique de jeunes suicidants: analyse du diagnostic psychiatrique initial, de l'observance thérapeutique et du taux de récurrence à un an (résultats préliminaires). Discussion: Le suicide. In <i>Annales médico-psychologiques</i> 1999;157:557–61.
Fleischmann 2008	N = 1867 participants, potentially eligible based on participants age (age 15–34)	Fleischmann A, Bertolote JM, Wasserman D, De Leo D, Bolhari J, Botega NJ, et al. Effectiveness of brief intervention and contact for suicide attempters: a randomized controlled trial in five countries. <i>Bull World Health Organ</i> 2008 Sep;86:703–9.
Gibbons 1978	N = 400 participants, potentially eligible based on participants age (age 17 +)	Gibbons JS, Butler J, Urwin P, Gibbons JL. Evaluation of a social work service for self-poisoning patients. <i>Br J Psychiatry</i> 1978 Aug;133:111–8.
Morgan 1993	N = 212 participants, potentially eligible based on participants age (age range not reported)	Morgan HG, Jones EM, Owen JH. Secondary prevention of non-fatal deliberate self-harm: the green card study. <i>Br J Psychiatry</i> 1993 Jul;163:111–2.
Motto 2001	N = 843 participants, potentially eligible based on participants age (age range not reported)	Motto JA, Bostrom AG. A randomized controlled trial of postcrisis suicide prevention. <i>Psychiatr Serv</i> 2001 Jun;52:828–33.
Wei 2013	N = 239 participants, potentially eligible based on participants age (age 15 +)	Wei S, Liu L, Bi B, Li H, Hou J, Tan S, et al. An intervention and follow-up study following a suicide attempt in the emergency departments of four general hospitals in Shenyang, China. <i>Crisis</i> 2013;34:107.
Welu 1977	N = 120 participants, potentially eligible based on participants age (age 16 +)	Welu TC. A follow-up program for suicide attempters: evaluation of effectiveness. 1977 Mar;7:17–30. N = 120 participants, potentially eligible based on participants age (age 16 +)
Unconfirmed–data lost		
Bennewith 2002	N = 2277 participants, potentially eligible based on participants age (age 16 +)	Bennewith O, Stocks N, Gunnell D, Peters TJ, Evans MO, Sharp DJ. General practice based intervention to prevent repeat episodes of deliberate self harm: cluster randomised controlled trial. <i>BMJ</i> 2002 May 25;324:1254.
VanHeeringen 1995	N = 516 participants, potentially eligible based on participants age (age 15 +)	Van Heeringen C, Jannes S, Buylaert W, Henderick H, De Bacquer D, Van Remoortel J. The management of non-compliance with referral to out-patient after-care among attempted suicide patients: a controlled intervention study. <i>Psychol Med</i> 1995 Sep;25:963–70.
Vijayakumar 2011	N = 680 participants, potentially eligible based on participants age (age 12 +)	Vijayakumar L, Umamaheswari C, Ali ZS, Devaraj P, Kesavan K. Intervention for suicide attempters: a randomized controlled study. <i>Indian J Psychiatry</i> 2011 Jul;53:244.
Ongoing study–not yet completed		
Martinique 2017	N = 260 participants, potentially eligible based on participants age (age 16 +), study still collecting follow-up data when contacted	<i>Suicide Prevention Algorithm in the French Overseas Territories (APSOM)</i> https://clinicaltrials.gov/ct2/show/NCT03427190
Slctr 2017	N = 300 participants, potentially eligible based on participants age (age 16 +), study still at analysis and writing up stage when contacted	A brief intervention for prevention of repetition of self-harm, among those who have recently attempted self-poisoning – a randomized controlled trial https://slctr.lk/trials/630

