BMC Psychiatry

RESEARCH

Open Access

Comparative efficacy and acceptability of psychotherapeutic, pharmacological, and combination treatments for non-suicidal self-injury in children and adolescents: a systematic review and network meta-analysis

Xinyi Chen[1,2†], Yingying Dong[1†], Mengfei Ye[1†], Xiang Wang[2], Junwei Yan[2,3], Yiying Yao[2], Zhihua Qi[4], Chao Qian[1*] and Zheng Liu[2*]

Abstract

Background Non-suicidal self-injury (NSSI) is a common and serious injury behavior in children and adolescents, however, its treatment remains controversial. Here, using network meta-analysis (NMA), we compared and ranked all available therapeutic treatment interventions to explore the best treatment strategy for NSSI in children and adolescents.

Methods We searched PubMed, Embase, the Cochrane Library and PsycINFO for randomized controlled trials used to reduce the frequency of NSSI in children and adolescents from database inception until Jan. 11, 2025. Primary outcomes were efficacy and acceptability. We estimated summary odds ratios (ORs) with credible intervals (CIs) in random effects models.

Results We included 28 trials comprising 6496 participants. Dialectical behavior therapy (DBT) was better than other interventions. In subgroup analysis, pharmacotherapy and psychotherapy significantly aggravated the frequency of NSSI in depression (OR = 1.53; 95% CI: 1.10 to 2.14); however, these interventions significantly reduced NSSI in patients with self-harm (OR = 0.53; 95% CI: 0.30 to 0.96). We also found that NSSI was significantly increased in the first 3 months when using SSRIs in treatment but was significantly reduced after 3 months.

Conclusion Psychotherapy seems to be a better choice than pharmacotherapy, especially DBT. DBT was associated with a better reduction in the frequency of NSSI than treatment as usual, with high confidence of evidence. NSSI is frequently used to combat depression symptoms, suggesting that clinicians should pay greater attention to depression symptoms to reduce NSSI, especially in the first 3 months of treatment with SSRIs.

Keywords Non-suicidal self-injury, Psychotherapy, Pharmacotherapy, Efficacy, Acceptability, Network meta-analysis

†Xinyi Chen, Yingying Dong and Mengfei Ye contributed equally to this work.

*Correspondence:
Chao Qian
qianchao5097@163.com
Zheng Liu
liuzheng1707@163.com
Full list of author information is available at the end of the article

Introduction

Non-suicidal self-injury (NSSI) behavior is a serious problem that often begins in adolescence, and its prevalence is highest during this stage of life. Rates of NSSI are notably elevated among younger people, including adolescents (17–27%) [64, 85, 100] and young adults (13–18%) [53, 85], especially among psychiatric inpatients (12–80%) [47, 54, 66]. An estimated 70% of adolescent psychiatric inpatients engage in NSSI [82]. It is noteworthy that NSSI is associated with the co-occurrence [4, 59, 67] and prediction [6, 97] of suicidal thoughts and behaviors. Among people with a history of NSSI, 55–85% report suicidal behaviors [25, 31]. Higher frequencies of NSSI are associated with an increased risk of suicide attempts [38], and suicide attempts could be developed via NSSI [36]. Despite the clinical seriousness and prevalence of NSSI among adolescents in medical and mental health settings, there are few studies on the efficacy of NSSI treatment and there are no standardized methods to deal with NSSI in adolescents [70].

Presently, various psychotherapies and pharmacotherapies have been proposed to treat NSSI, which are based on treatments for other psychiatric disorders [89]. Many studies show that dialectical behavioral therapy (DBT) [55], the best-known evidence-based psychotherapy, can lead to greater reductions in the frequency of NSSI and number of NSSI instances [62, 71, 77]. Previous meta-analyses have also confirmed that adolescents exhibit fewer NSSI following a course of DBT [19]. Cognitive Behavioral Therapy (CBT is another proven therapy to treat depression,however, some research shows that CBT does not reduce NSSI in the treatment of adolescent depression [13, 35, 97] and even increases the risk of engaging in NSSI [13]. Because of the increasing interest in psychotherapy for NSSI [13, 45, 69, 89], treatments have recently been developed focusing on NSSI in children and the adolescent population. For instance, treatment for self-injurious behaviors [1–3], emotional regulation individual therapy for adolescents [10–12], cutting down program [26, 32, 50, 88], and developmental group psychotherapy (DGP) [37, 99] have shown positive effects on reducing NSSI. Among pharmacotherapies, whether selective serotonin reuptake inhibitors (SSRIs) can reduce the frequency of NSSI remains controversial. Uncontrolled trials have shown the benefits of fluoxetine in reducing the frequency of NSSI, but replication in controlled trials to support these findings is lacking [89, 89]. In contrast, other studies have found that SSRIs tend to increase the frequency of NSSI, although the results are statistically non-significant [27, 81].

According to past studies, whether psychotherapy or pharmacotherapy can actually reduce NSSI has not been proven by sufficient evidence for the following reasons. First, the terminology of NSSI lacks clarity due to different theoretical and clinical environments, with a wide range of related terms (e.g., deliberate self-injury, intentional injury) [18, 34, 40, 52, 80] [18, 34, 40], and some studies even involve a broader category of behaviors, including both suicidal self-injury (SSI) and NSSI [49]. Second, NSSI is often comorbid with other psychiatric disorders, such as borderline personality disorder (BPD) or depression; therefore, few current treatments have assessed the effectiveness of treatment specially designed to reduce NSSI; most treatments are based on treatments to address other psychiatric disorders. Third, previous meta-analyses [19, 27, 69, 70, 98] have typically provided separate coverage for pharmacotherapies and psychotherapies, and most studies have been based on small samples, with a small number of studies and nonrandomized designs [19, 70], which limits the choice of treatment and the precision in estimating individual study effect sizes. Thus, although NSSI is a common phenomenon among adolescents, clinicians be unsure whether there are effective and acceptable treatment options for adolescents affected by NSSI or those who are at high risk of NSSI.

Network meta-analysis (NMA) is a sophisticated method that enables the simultaneous comparison of multiple treatments by integrating both direct and indirect evidence sources within a single analytical framework. This approach allows for the pooling of samples across numerous small randomized controlled trials (RCTs), thereby enhancing the statistical power to detect differences in outcomes. NMAs may offer advantages over standard meta-analyses in certain scenarios, as the indirect comparisons within the network can help to mitigate study-specific biases that may not be apparent in head-to-head RCTs. Furthermore, a NMA can incorporate a broader range of data into the analysis, enabling researchers to address the bigger picture, whereas a traditional meta-analysis often provides a more fragmented view.

To ensure our findings pertain specifically and uniquely to NSSI, in the present study, the definition of NSSI used refers to intentional and socially unacceptable behavior, aiming to cause destruction or impairment of bodily tissues but with only slight or moderate physical injury, and with no conscious suicidal intention. Meanwhile, utilizing NMA, our objective was to provide comprehensive and hierarchical evidence regarding the efficacy and acceptability of pharmacotherapy, psychotherapy, and proposed combined therapies in reducing the frequency of NSSI among children and adolescents with comorbid psychiatric disorders.

Methods

The detailed methods followed in this systematic review and NMA are described in the study protocol registered a priori at PROSPERO (CRD42024510039). In reporting the results, we followed the PRISMA extension statement for NMA.

Search strategy and selection criteria

We searched PubMed, Embase, the Cochrane Library and PsycINFO for eligible RCTs published from database inception to Jan. 11, 2025. We only extracted data from phase 1 in open-label or crossover studies to avoid biases caused by differences in treatment regimens received by patients across different phases. We defined NSSI as any self-injury, including self-poisoning and self-cutting without suicidal intent. To maximize comprehensiveness, studies considered eligible for inclusion were those that reported information on the frequency of NSSI for children and adolescents treated with any active intervention, with any control condition or another active intervention in RCTs, whether studies of treatment directly targeting NSSI or treatment based on treatments for other psychiatric disorders. PICO (population, intervention, comparison, and outcome) was used to assess article eligibility.

Population

Studies were included if they reported the frequency of NSSI among children and adolescents (≤25 years old). We excluded studies with no control group, those with fewer than 10 participants per group, and a diagnosis of autism-spectrum or other neurodevelopmental disorders. Data were requested from the corresponding authors or searched for in other reviews and meta-analyses when the data could not be retrieved from the original publications. The language was restricted to English.

Intervention

Pharmacotherapies including SSRIs (escitalopram, fluoxetine, paroxetine, and sertraline), serotonin norepinephrine reuptake inhibitors (duloxetine, atomoxetine, venlafaxine, and desvenlafaxine), and other drugs (guanfacine extended-release), as well as any manualized or structured psychotherapies including cognitive analytic therapy (CAT), CBT, DBT, DGP, emotion regulation training (ERT), family therapy, iconic therapy, mentalization-based treatment, and supportive therapy, regardless of the delivery format (e.g., individual or group) or treatment medium (e.g., face-to-face or online). We included combined pharmacotherapies and psychotherapies. In addition to the above interventions, we also included some brief interventions (hospital admission tokens and brief app-based interventions). To facilitate our analyses, we merged some interventions. For example, variants of an established modality were collapsed into the main classification (e.g., family-focused CBT was collapsed into CBT, DBT for adolescents was collapsed into DBT, therapeutic assessment was collapsed into CAT, and family enhanced non-directive supportive therapy was collapsed into supportive therapy).

Comparison

The control conditions were placebo, treatment as usual (TAU), and no treatment. We merged enhanced usual care and good clinical care into TAU. All comparisons were based on elimination of the common therapy framework. We merged the types that did not receive any intervention after eliminating the common therapy framework and as assessment as usual [68], which also did not receive any treatment into no treatment.

Outcomes

Primary outcomes were efficacy (frequency of NSSI after treatment) and acceptability (all-cause discontinuation measured as the proportion of patients who discontinued treatment up to the post-intervention time point). For studies that reported outcomes at more than one point in time, maximum follow-up outcome data were extracted.

Data extraction

One author (X.C.) independently extracted key information from the included studies using a data collection form to record information against the outcome measures. Data were confirmed by consultation with the other review authors.

The following data were collected from each study: study characteristics (first author of study, country of study, sample size), participant characteristics (gender, age, the main diagnosis of disease and diagnostic criteria), experimental and control group characteristics (type of intervention, treatment duration and measurement), and outcomes (the frequency of NSSI after treatment, all-cause discontinuation measured by the proportion of patients who discontinued treatment up to the post-intervention time point).

Data analysis

We conducted NMA and pairwise meta-analysis in Stata version 17.0 [43] using the random-effects model with summary odds ratios (ORs) and 95% confidence intervals (CIs) for dichotomous outcomes. Considering the very small number of NSSI events, some studies have even reported no NSSI events with some treatments, which would have a large impact on our results. We processed these results, adding one to results with zero NSSI events, and adding one after doubling the total events [86]. We conducted frequentist random effects meta-analyses

for all direct treatment comparisons, allowing for heterogeneity in treatment effects between studies. The proportion of the total variance within each pairwise comparison that is owing to between-study heterogeneity was estimated using the I^2 statistic [42]. We also report the heterogeneity variance Tau^2 for each pairwise comparison as a measure of heterogeneity that is independent of sample size. We performed sensitivity analyses to assess the relative impact of each individual study on the pooled effect size.

Risk of bias and confidence in evidence assessment

Two researchers (X.C. and X.W) independently selected the studies, reviewed the main reports and supplementary materials, extracted the relevant information from the included trials, and assessed the risk of bias in included studies, according to the Cochrane Handbook for Systematic Reviews of Interventions. Disagreements among the researchers in specific studies were resolved in discussion, with the participation of a third investigator where necessary. The level of risk of bias in each of these domains was presented separately for each study in tables in the final publication. We assessed the confidence of evidence contributing to each network estimate using Confidence In Network Meta-Analysis (CINeMA) software [76].

Network meta-analysis

NMA is a new methodological approach that allows for the simultaneous comparison of multiple interventions within a single analysis while preserving randomization. This approach was applied to integrate direct evidence (from studies directly comparing interventions) with indirect evidence (information about two treatments derived via a common comparator) to estimate the comparative efficacy and acceptability of all treatments, resolving the limitations of previous studies. In contrast to pairwise meta-analysis, NMAs produced strong evidence against the null hypothesis more often and earlier. To visualize network geometry and node connectivity, we produced network plots for each outcome [14]. NMAs were fit within a frequentist framework using a multivariate random effects (restricted maximum likelihood estimation) meta-analysis model [43, 96] that accounts for the correlations between effect sizes in trials with more than two groups. We assumed network consistency and a common heterogeneity parameter across all treatment contrasts. For all treatment comparisons, we calculated summary ORs and 95% CIs that account for uncertainty in variance estimates [46] in league tables.

To obtain treatment hierarchies, we used a parametric bootstrap procedure with 10,000 resamples to estimate the ranking probabilities of being at each possible rank for each intervention. The treatment hierarchy was summarized and reported as surface under the cumulative ranking curve. We also present summary treatment effects with 95% CIs and 95% prediction intervals [14] for all placebo comparisons in forest plots. NMAs were conducted using the network [57] package in Stata (version 17.0). To assess transitivity, we compared age and sex, which could act as effect modifiers across treatment comparisons. We used comparison-adjusted funnel plots [14] and the Egger's regression test to assess publication bias. Assuming equivalence of direct and indirect evidence (e.g., consistency) in NMA might lead to inaccurate conclusions when there is evidence for statistically significant inconsistency [96]. Incoherence between direct and indirect sources of evidence was statistically assessed globally by comparison of the fit and parsimony of consistency and inconsistency models, and locally by calculation of the difference between direct and indirect estimates in all closed loops in the network [43]. The node splitting method, which separates evidence on a particular comparison into direct and indirect evidence, was used to calculate inconsistency of the model.

Subgroup analysis and meta-regression analysis

To determine whether the results were affected by study characteristics, we performed subgroup analysis for primary outcomes according to the following variables: psychiatric disorder, intervention, treatment duration and measurement. We chose active treatments (pharmacotherapy and psychotherapies) with control conditions (no treatment, placebo, TAU) for subgroup analysis. Because there is only one published study on combination intervention, we did not do subgroup analysis. Given that NSSI frequently co-occurs with other psychiatric disorders, we performed a subgroup analysis examining the comorbid psychiatric disorders in NSSI patients. This analysis aims to elucidate the incidence and associated patterns of NSSI within the spectrum of other psychiatric comorbidities. With psychiatric disorders, if patients were transdiagnostic, we analyzed them according to the main diagnosis. In patients with multiple primary diagnoses, we analyzed them in every main diagnosis group. We merged suicide- and self-harm-related behaviors as self-harm. Because rumination is closely associated with depression and anxiety and can increase the risk of depression and anxiety, we analyzed rumination in both depression and anxiety groups. The types of pharmacotherapy analyzed were classified as SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs), anti-attention-deficit/hyperactivity disorder (ADHD) medication; the types of psychotherapy analyzed were brief intervention, CBT, CAT, ERT, DBT, DGP, family therapy, and mentalization-based treatment. Considering that

suicide- and self-harm-related behaviors mostly occurred in the first 3 months of SSRIs treatment [24], we took 3 months as the cutoff for further analysis. We also analyzed measurement of NSSI. We classified studies that used less strict assessment instruments (clinical interview or self-report) to measure NSSI studies as "without a rating scale" and others were classified as "rating scale".

We also did meta-regression for primary outcomes according to sex (females/total), mean age, and treatment duration (Appendix 10).

Results

We identified 2044 citations, retrieved the full text of 203 potentially eligible articles, and included 28 RCTs with 6496 patients (Appendix 2). These trials comprised six pharmacotherapies, 10 psychotherapies, two combination interventions, and three control interventions. The mean study sample size was 203 participants and ranged from 40 to 488. The age range was from 6 to 25 years. In most studies (89.3%), females made up more than 50% of the total patients. Half of studies used less-strict assessment instruments (clinical interview or self-report) to measure NSSI. In studies on measuring NSSI with rating scales, 64.3% used the Columbia–Suicide Severity Rating Scale (C-SSRS). Further descriptive information about the included studies is given in Table 1.

Network meta-analysis

Concerning efficacy, in the comparisons between active treatment and control conditions, both DBT and iconic therapy were significantly superior to no treatment and TAU (ORs ranged from 0.03 to 0.19; Figs. 1A, 2, 3A). SSRIs + CBT and CBT were worse than placebo (ORs 4.32 and 5.18, respectively; Figs. 1A, 2, 3A). In comparisons between two active treatments, iconic therapy was better than most psychotherapies and one combination intervention (Figs. 1A, 2). CAT and CBT were worse than DBT (ORs 4.94 and 8.46, respectively; Figs. 1A, 2). Desvenlafaxine was significantly superior to CBT and SSRIs + CBT (ORs 0.13 and 0.15, respectively; Figs. 1A, 2).

Concerning acceptability, in comparisons between two control conditions, no treatment had fewer all-cause NSSI discontinuations than placebo (OR = 0.29; 95% CI: 0.15 to 0.58; Figs. 1B, 2, 3B). In the comparisons between active treatment and control conditions, all pharmacotherapies, ERT and all combination interventions (SSRIs + CBT and VEN + CBT) were associated with significantly more NSSI discontinuations than no treatment (ORs range from 2.47 to 20.03), and DGP was associated with significantly fewer discontinuations than no treatment (OR = 0.48; 95% CI: 0.31 to 0.74; Figs. 1B, 2, 3B). Brief intervention, CAT, CBT, and DGP were associated with significantly fewer NSSI discontinuations than placebo (ORs range from 0.14 to 0.29) whereas ERT was associated with significantly more discontinuations than placebo (OR = 5.83; 95% CI: 1.11 to 30.69; Figs. 1B, 2, 3B). CAT was associated with significantly fewer NSSI discontinuations than TAU (OR = 0.40; 95% CI: 0.18 to 0.89), and ERT was associated with more discontinuations than TAU (OR = 13.98; 95% CI: 2.11 to 92.84; Figs. 1B, 2, 3B). In comparisons between two active treatments, CAT, CBT, and DGP were associated with the fewest NSSI discontinuations (Figs. 1B, 2). By contrast, the most active treatments had fewer all-cause discontinuations than ERT (ORs ranged from 0.02 to 0.19; Figs. 1B, 2, and Appendix 6).

We did not found any significant incoherence for efficacy and the acceptability in the test of global incoherence, tests of local incoherence and the test of the node-splitting model (Appendix 8). The assessment of transitivity showed most comparisons had a mean age and sex ratio (Appendix 7). Comparison-adjusted funnel plots of the NMA and Egger's regression tests were not suggestive of publication bias for efficacy and acceptability outcome (Appendix 9). The finding that the primary outcomes were robust was substantiated by the fact that there was no alteration in the statistical significance when a sensitivity analysis was conducted by sequentially removing each study individually (Appendix 10).

Subgroup analysis and meta-regression analysis

Concerning efficacy, subgroup analysis showed that with psychiatric disorders, pharmacotherapy and psychotherapy tended to aggravate the frequency of NSSI in patients with depression and ADHD, especially depression (OR = 1.53; 95% CI: 1.10 to 2.14; Fig. 4). However, in patients with anxiety, self-harm, and BPD, those interventions tended to reduce NSSI, especially in those with self-harm (OR = 0.53; 95% CI: 0.30 to 0.96; Fig. 4). For pharmacotherapy, anti-ADHD medication and SSRIs tended to increase the frequency of NSSI. In further analyses, we found that NSSI was significantly increased in the first 3 months when using SSRIs for treatment (OR = 1.97; 95% CI: 1.01 to 3.81) and significantly reduced after 3 months (OR = 0.09; 95% CI: 0.02 to 0.47; Fig. 4). In meta-regression analysis, we found that the frequency of NSSI was significantly related with the duration of treatment when using SSRIs for therapy ($P = 0.037$; Fig. 4). Psychotherapy tended to reduce NSSI, in general, especially DBT (OR = 0.08; 95% CI: 0.03 to 0.25) and mentalization-based treatment (OR = 0.26; 95% CI: 0.09 to 0.78); CBT seemed to have the opposite tendency (Fig. 4). We found no significant differences regarding whether to use

Table 1 Randomized controlled trials included in the systematic review and network meta-analysis. All comparisons are based on elimination of the common therapy framework. After eliminating the common therapy framework, the groups did not receive any intervention. References for included studies are provided in the Appendix 3

References (author,year)	Country	Sample size	Clinical group (main diagnosis)	Diagnostic criteria	Female (%)	Years, mean(SD)	Age range	Test group	Control group	Common therapy Framework	Measurement	Treatment duration
Atkinson et al., (2018) [7]	USA	486	Transdiagnostic (MDD)	DSM-IV-TR	56.47%	13.03(2.84)	7 ~ 17	DEV	Placebo	—	C-SSRS	8 w
Atkinson et al., (2014)[a] [8]	USA	337	MDD	DSM-IV-TR	52.23%	13.16(3.14)	7 ~ 17	DUL DUL SSRIs	SSRIs Placebo Placebo	— — —	C-SSRS	10w
Brent et al., (2009) [13]	USA	334	Transdiagnostic (MDD)	DSM-IV	69.76%	15.90(1.55)	12 ~ 18	CBT VEN VEN VEN + CBT VEN CBT	— SSRIs SSRIs + CBT SSRIs SSRIs —	VEN — — — CBT SSRIs	Self-report	12w
Chanen et al., (2008)[c] [15]	Australia	98	BPD	DSM–IV	75.64%	16.4 (0.9)	15 ~ 18	CAT	TAU	—	Clinical interview	24 mo
Cotgrove et al., (1995)[c] [20]	UK	105	Suicide attempts	NA	84.76%	14.9	12.2 ~ 16.7	BI	—	AAU	Clinical records	12mo
Davey et al., (2019) [22]	Australia	153	MDD	DSM-IV	58.82%	19.6(2.7)	15 ~ 25	SSRIs	Placebo	CBT	C-SSRS	12 w
Diamond et al., (2019)[b] [23]	USA	129	Transdiagnostic (suicide,depression)	BDI-II and SIQ-JR	81.20%	14.87(1.68)	12 ~ 18	FT	ST	—	C-SSRS	16 w
Emslie et al., (2009) [28]	USA	312	MDD	DSM-IV	58.97%	14.6(1.55)	12 ~ 17	SSRIs	Placebo	—	Clinical records and self-report	8 w
Emslie et al., (2014)[a] [29]	USA	463	MDD	DSM-IV-TR	51.19%	12.98(2.98)	7 ~ 17	DUL DUL SSRIs	SSRIs Placebo Placebo	— — —	C-SSRS	10w
Esposito Smythers et al., (2019) [30]	USA	147	Transdiagnostic (MDD,suicidal crisis)	DSM-IV-TR	76.19%	14.9(1.51)	12 ~ 18	CBT	TAU	—	SITBI	12mo
Goodyer et al., (2007) [35]	UK	208	Transdiagnostic (depression)	K-SADS-PL	74.04%	NA median: 14	11 ~ 17	CBT	—	SSRIs	K-SADS-PL	28w
Green et al., (2011)[c] [37]	UK	366	Self-harm	NA	88.52%	NA	12 ~ 17	DGP	—	TAU	Clinical interview	12mo
Harrington et al., (1998)[c] [39]	UK	162	Deliberate self-poisoning,Self-harm	NA	89.51%	14.50(1.16)	10 ~ 16	FT	—	TAU	Clinical interview	NA
Hervas et al., (2014) [41]	Spain	337	Transdiagnostic (ADHD)	ADHD-RS-IV	26.11%	10.80(2.79)	6 ~ 17	GXR GXR ATX	ATX Placebo Placebo	— — —	C-SSRS	12 ~ 15w

Table 1 (continued)

References (author,year)	Country	Sample size	Clinical group (main diagnosis)	Diagnostic criteria	Female (%)	Years, mean(SD)	Age range	Test group	Control group	Common therapy Framework	Measurement	Treatment duration
Hurtado-Santiago et al., (2022)[d] [44]	Spain	40	Transdiagnostic (BPD,Suicide)	C-SSRS, CEPER-III-BPD	82.50%	20.53(4.32)	15 ~ 25	ST	IT	TAU	NA	10 ~ 12w
Kennard et al., (2018) [51]	USA	66	Suicide	NA	89.40%	15.1(1.5)	12 ~ 18	BI	—	g	C-SSRS	24w
McCauley et al., (2018) [60]	USA	173	Transdiagnostic (suicide,BPD)	SIQ-JR, DSM-IV	94.22%	14.89(1.47)	15 ~ 25	DBT	ST	—	SASII	6mo
Mehlum et al., (2014)[c] [62]	Norway	77	Transdiagnostic (Self-harm,BPD)	DSM-IV	88.31%	15.6(1.5)	12 ~ 18	DBT	TAU	—	Self-reported	19w
Melvin et al., (2019) [63]	Australia	59	Transdiagnostic (Anxiety)	DSM-IV-TR	45.76%	13.59 (1.08)	10 ~ 16.5	SSRIs Placebo SSRIs	— — Placebo	CBT CBT CBT	SEFCA	6mo
Ougrin et al., (2013)[c] [68]	UK	107	Self-harm	NA	80.00%	15.55(1.36)	12 ~ 18	CAT	AAU	—	Clinical records	NA
Rossouw et al., (2012)[c] [75]	UK	80	Self-harm	NA	85.00%	15.1(1.29)	12 ~ 17	MBT	TAU	—	Clinical interview and self-report	12mo
Schuppert et al., (2009)[c] [78]	Netherlands	43	Transdiagnostic (BPD)	DSM-IV	88.37%	16.14(1.23)	14 ~ 19	ERT	—	TAU	Clinical interview and self-report	17w
Schuppert et al., (2012)[c] [79]	Netherlands	109	Transdiagnostic (BPD)	DSM-IV	96.33%	15.98(1.22)	14 ~ 19	ERT	—	TAU	Clinical interview and self-report	17w
Strawn et al., (2015)[a] [84]	USA	272	Transdiagnostic (Anxiety)	DSM-IV-TR	53.31%	12.40(2.96)	7 ~ 17	DUL	Placebo	—	C-SSRS	10w
Walkup et al., (2008) [92]	USA	488	Transdiagnostic (Anxiety)	DSM-IV-TR	49.59%	10.65(2.83)	7 ~ 17	CBT SSRIs SSRIs + CBT SSRIs SSRIs CBT	— — Placebo CBT Placebo Placebo	SSRIs CBT — — — —	Clinical interview	12w
Webb et al., (2022)[b] [93]	USA	152	Rumination	CRSQ	58.55%	13.71(0.90)	12 ~ 15	BI	AAU	—	Self-reported	3w
Weihs et al., (2018) [94]	USA	339	Transdiagnostic (MDD)	DSM-IV-TR	54.28%	12.73(2.99)	7 ~ 17	SSRIs SSRIs DEV	DEV Placebo Placebo	— — —	C-SSRS	8w
Wood et al., (2001)[c] [99]	UK	63	Deliberate self-harm	NA	77.78%	14.25(1.67)	12 ~ 16	DGP	—	TAU	Clinical intreview	6mo

Table 1 (continued)

ADHD Attention-deficit/hyperactivity disorder, *ADHD-RS-IV* ADHD Rating Scale version IV, *ATX* Atomoxetine, *BDI-II* Beck Depression Inventory-II, *BI* Brief intervention, *BPD* Borderline personality disorder, *CAT* Cognitive analytic therapy, *CBT* Cognitive behavioral therapy, *CEPER-III-BPD* Exploratory Questionnaire of Personality-III-BPD, *CRSQ* Children's Response Styles Questionnaire, *C-SSRS* Columbia–Suicide Severity Rating Scale, *DBT* Dialectical behavior therapy, *DEV* Desvenlafaxine, *DGP* Developmental group psychotherapy, *DUL* Duloxetine, *ERT* Emotion regulation training, *FT* Family therapy, *GXR* Guanfacine extended-release, *IT* Iconic therapy, *K-SADS-PL* Kiddie Schedule for affective disorders and schizophrenia present and lifetime version, *MBT* Mentalization-based treatment, *MDD* Major depressive disorder, *NT* No treatment, *PBO* Placebo, *SASII* Suicide Attempt Self-Injury Interview, *SEFCA* Side-effects Form for Children and Adolescents, *SIQ-JR* Suicidal Ideation Questionnaire-Junior, *SITBI* Self-injurious thoughts and behavior interview, *SSRIs* Selective serotonin reuptake inhibitors, *SSRIs + CBT* Selective serotonin reuptake inhibitors plus cognitive behavioral therapy, *ST* Supportive Therapy, *TAU* Treatment as usual, *VEN* Venlafaxine, *VEN + CBT* Venlafaxine plus cognitive behavioral therapy

[a] Only data from phase 1 in multiphase studies extracted. [b]Data from trial registers with results were posted. [c]Data were provided in a high-quality published meta-analysis[69]. [d]Investigators recruited participants aged 15 to 25 years instead of 15 to 30 years, as initially planned

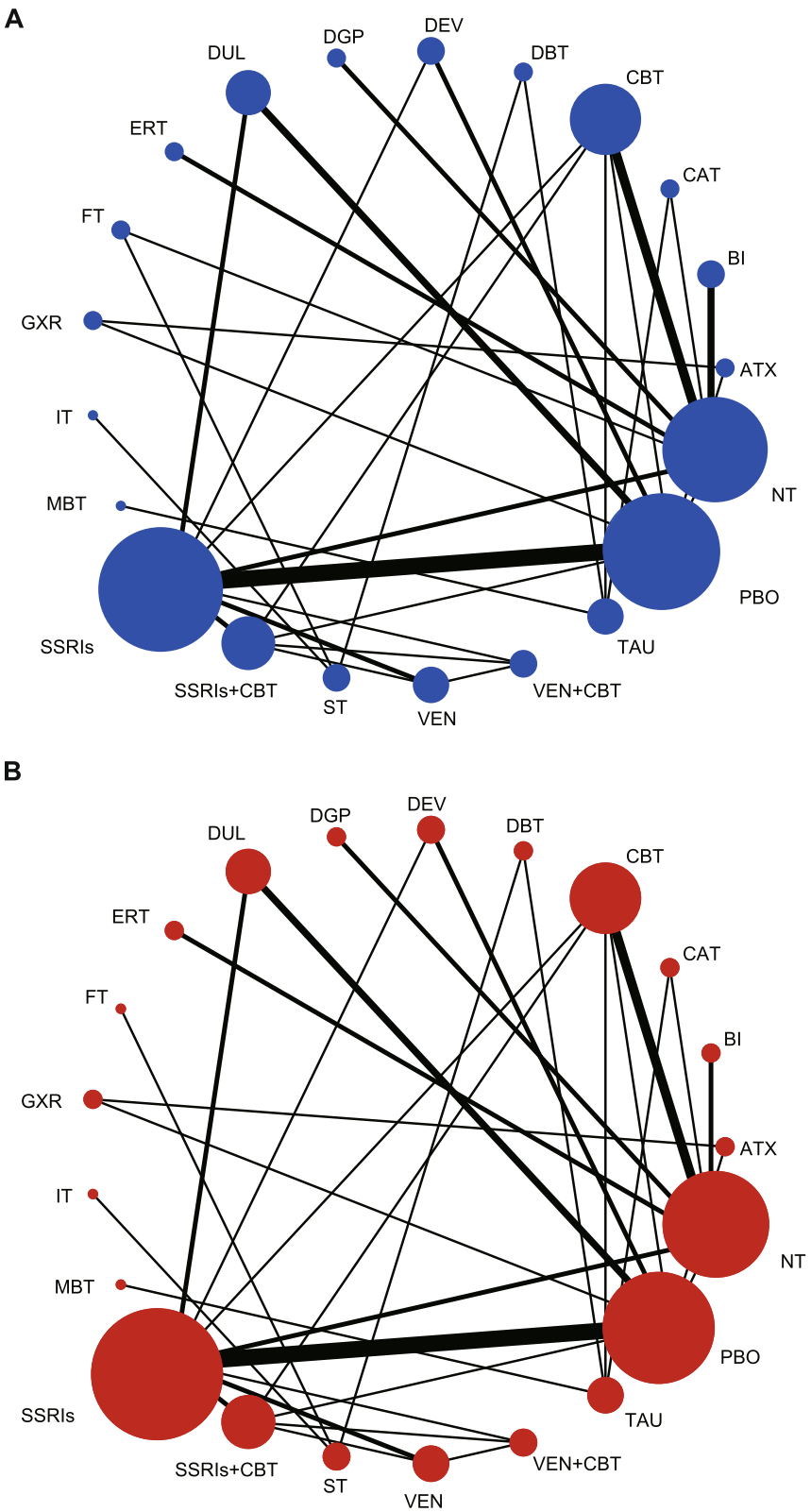


Fig. 1 Network of eligible comparisons. **A** Efficacy. B Acceptability. The width of the lines is proportional to the number of trials comparing every pair of treatments, and the size of each node is proportional to the number of randomly assigned participants

ATX	1.18 (0.54 to 2.60)	1.15 (0.55 to 2.40)	1.02 (0.53 to 1.95)	1.40 (0.68 to 2.89)	1.49 (0.64 to 3.50)	**5.46 (1.11 to 26.73)**	**7.57 (1.51 to 37.88)**	**4.26 (1.62 to 11.16)**	3.54 (0.60 to 20.88)	**8.93 (3.11 to 25.69)**	0.21 (0.04 to 1.29)	1.26 (0.15 to 10.22)	3.77 (0.38 to 37.39)	4.06 (0.74 to 22.39)	1.32 (0.20 to 8.75)	1.74 (0.75 to 4.03)	1.12 (0.45 to 2.80)	**4.30 (1.63 to 11.30)**	1.25 (0.64 to 2.45)	3.00 (0.69 to 12.95)
6.04 (0.36 to 101.64)	DEV	0.97 (0.59 to 1.59)	0.86 (0.39 to 1.89)	1.18 (0.75 to 1.87)	1.26 (0.67 to 2.39)	**4.61 (1.04 to 20.39)**	**6.39 (1.41 to 28.95)**	**3.59 (1.64 to 7.89)**	2.99 (0.55 to 16.12)	**7.54 (3.07 to 18.49)**	**0.18 (0.03 to 0.99)**	1.06 (0.14 to 8.00)	3.18 (0.34 to 29.47)	3.42 (0.68 to 17.21)	1.12 (0.18 to 6.79)	1.47 (0.78 to 2.75)	0.94 (0.46 to 1.96)	**3.63 (1.65 to 7.99)**	1.06 (0.71 to 1.58)	2.53 (0.65 to 9.79)
2.63 (0.18 to 38.65)	0.44 (0.09 to 2.02)	DUL	0.89 (0.43 to 1.85)	1.22 (0.88 to 1.68)	1.30 (0.75 to 2.25)	**4.74 (1.11 to 20.30)**	**6.57 (1.50 to 28.83)**	**3.70 (1.80 to 7.60)**	3.08 (0.59 to 16.10)	**7.76 (3.35 to 17.98)**	**0.19 (0.03 to 0.99)**	1.09 (0.15 to 8.04)	3.27 (0.36 to 29.66)	3.52 (0.72 to 17.18)	1.15 (0.19 to 6.80)	1.51 (0.88 to 2.60)	0.97 (0.50 to 1.87)	**3.73 (1.81 to 7.71)**	1.09 (0.81 to 1.46)	2.61 (0.70 to 9.71)
2.05 (0.16 to 25.95)	0.34 (0.01 to 7.92)	0.78 (0.04 to 16.10)	GXR	1.37 (0.66 to 2.83)	1.46 (0.63 to 3.42)	**5.34 (1.09 to 26.15)**	**7.40 (1.48 to 37.05)**	**4.16 (1.59 to 10.91)**	3.47 (0.59 to 20.43)	**8.74 (3.04 to 25.12)**	0.21 (0.03 to 1.26)	1.23 (0.15 to 10.00)	3.69 (0.37 to 36.57)	3.97 (0.72 to 21.90)	1.29 (0.20 to 8.56)	1.70 (0.73 to 3.94)	1.09 (0.44 to 2.74)	**4.20 (1.60 to 11.05)**	1.22 (0.62 to 2.40)	2.93 (0.68 to 12.67)
2.19 (0.16 to 29.82)	0.36 (0.09 to 1.42)	0.83 (0.32 to 2.16)	1.07 (0.06 to 20.60)	SSRIs	1.07 (0.68 to 1.68)	3.90 (0.94 to 16.18)	**5.40 (1.27 to 23.01)**	**3.04 (1.57 to 5.87)**	2.53 (0.50 to 12.89)	**6.37 (2.90 to 14.01)**	**0.15 (0.03 to 0.79)**	0.90 (0.12 to 6.46)	2.69 (0.30 to 23.90)	2.90 (0.61 to 13.74)	0.94 (0.16 to 5.46)	1.24 (0.79 to 1.95)	0.80 (0.45 to 1.42)	**3.07 (1.58 to 5.95)**	0.89 (0.68 to 1.16)	2.14 (0.59 to 7.72)
2.23 (0.14 to 35.32)	0.37 (0.07 to 1.90)	0.85 (0.23 to 3.15)	1.09 (0.05 to 24.00)	1.02 (0.40 to 2.57)	VEN	3.65 (0.82 to 16.18)	**5.06 (1.12 to 22.96)**	**2.85 (1.30 to 6.26)**	2.37 (0.44 to 12.78)	**5.98 (2.43 to 14.68)**	**0.14 (0.03 to 0.79)**	0.84 (0.11 to 6.35)	2.52 (0.27 to 23.37)	2.71 (0.54 to 13.65)	0.88 (0.14 to 5.39)	1.16 (0.67 to 2.00)	0.75 (0.41 to 1.37)	**2.87 (1.30 to 6.35)**	0.84 (0.50 to 1.40)	2.01 (0.52 to 7.77)
1.42 (0.07 to 27.83)	0.23 (0.03 to 1.73)	0.54 (0.09 to 3.16)	0.69 (0.03 to 18.51)	0.65 (0.14 to 3.06)	0.63 (0.11 to 3.76)	BI	1.39 (0.22 to 8.63)	0.78 (0.21 to 2.87)	0.65 (0.09 to 4.68)	1.64 (0.43 to 6.19)	**0.04 (0.01 to 0.28)**	0.23 (0.02 to 2.23)	0.69 (0.06 to 8.03)	0.74 (0.11 to 5.05)	0.24 (0.03 to 1.94)	0.32 (0.07 to 1.39)	**0.20 (0.04 to 0.94)**	0.79 (0.22 to 2.78)	**0.23 (0.05 to 0.97)**	0.55 (0.10 to 3.01)
1.34 (0.07 to 27.33)	0.22 (0.03 to 1.73)	0.51 (0.08 to 3.19)	0.65 (0.02 to 18.11)	0.61 (0.12 to 3.11)	0.60 (0.09 to 3.78)	0.94 (0.23 to 3.95)	CAT	0.56 (0.15 to 2.06)	0.47 (0.13 to 1.70)	1.18 (0.29 to 4.74)	**0.03 (0.00 to 0.21)**	**0.17 (0.03 to 0.92)**	0.50 (0.07 to 3.49)	0.54 (0.16 to 1.78)	**0.17 (0.04 to 0.74)**	0.23 (0.05 to 1.02)	**0.15 (0.03 to 0.70)**	0.57 (0.15 to 2.13)	**0.17 (0.04 to 0.71)**	**0.40 (0.18 to 0.89)**
0.78 (0.04 to 13.72)	**0.13 (0.02 to 0.80)**	0.30 (0.06 to 1.43)	0.38 (0.02 to 9.23)	0.36 (0.09 to 1.34)	0.35 (0.07 to 1.69)	0.55 (0.18 to 1.73)	0.58 (0.19 to 1.84)	CBT	0.83 (0.19 to 3.71)	**2.10 (1.22 to 3.60)**	**0.05 (0.01 to 0.24)**	0.30 (0.05 to 1.91)	0.88 (0.11 to 7.13)	0.95 (0.23 to 3.93)	0.31 (0.06 to 1.59)	**0.41 (0.19 to 0.87)**	**0.26 (0.11 to 0.62)**	1.01 (0.72 to 1.41)	**0.29 (0.15 to 0.59)**	0.70 (0.23 to 2.13)
6.54 (0.29 to 148.25)	1.08 (0.12 to 9.80)	2.49 (0.34 to 18.43)	3.19 (0.10 to 97.38)	2.99 (0.49 to 18.24)	2.93 (0.39 to 21.79)	4.62 (0.90 to 23.85)	**4.89 (1.11 to 21.61)**	**8.38 (2.14 to 32.91)**	DBT	2.52 (0.52 to 12.24)	**0.06 (0.01 to 0.52)**	0.36 (0.12 to 1.08)	1.06 (0.25 to 4.56)	1.15 (0.30 to 4.36)	**0.37 (0.19 to 0.72)**	0.49 (0.09 to 2.61)	0.32 (0.06 to 1.76)	1.21 (0.26 to 5.55)	0.35 (0.07 to 1.82)	0.85 (0.31 to 2.31)
2.05 (0.10 to 40.43)	0.34 (0.05 to 2.49)	0.78 (0.13 to 4.66)	1.00 (0.04 to 26.89)	0.94 (0.20 to 4.39)	0.92 (0.15 to 5.48)	1.45 (0.39 to 5.32)	1.53 (0.38 to 6.20)	2.62 (0.87 to 7.89)	0.31 (0.06 to 1.54)	DGP	**0.02 (0.01 to 0.12)**	**0.14 (0.02 to 0.97)**	0.42 (0.05 to 3.61)	0.45 (0.10 to 2.05)	**0.15 (0.03 to 0.82)**	**0.19 (0.08 to 0.47)**	**0.13 (0.05 to 0.33)**	**0.48 (0.31 to 0.74)**	**0.14 (0.06 to 0.32)**	0.34 (0.10 to 1.14)
1.52 (0.08 to 30.19)	0.25 (0.03 to 1.88)	0.58 (0.10 to 3.46)	0.74 (0.03 to 20.07)	0.69 (0.15 to 3.33)	0.68 (0.11 to 4.10)	1.08 (0.28 to 4.07)	1.14 (0.27 to 4.78)	1.95 (0.62 to 6.15)	0.23 (0.05 to 1.20)	0.74 (0.21 to 2.62)	ERT	5.87 (0.52 to 65.64)	**17.57 (1.32 to 234.27)**	**18.92 (2.34 to 152.67)**	6.16 (0.66 to 57.89)	**8.10 (1.49 to 43.95)**	5.21 (0.92 to 29.64)	**20.03 (4.43 to 90.53)**	**5.83 (1.11 to 30.69)**	**13.98 (2.11 to 92.84)**
1.89 (0.09 to 38.87)	0.31 (0.04 to 2.46)	0.72 (0.11 to 4.55)	0.92 (0.03 to 25.75)	0.86 (0.17 to 4.44)	0.85 (0.13 to 5.40)	1.34 (0.32 to 5.56)	1.42 (0.34 to 5.97)	2.42 (0.72 to 8.14)	0.29 (0.08 to 1.10)	0.92 (0.23 to 3.71)	1.24 (0.30 to 5.19)	FT	3.00 (0.62 to 14.58)	3.23 (0.57 to 18.38)	1.05 (0.43 to 2.59)	1.38 (0.19 to 10.30)	0.89 (0.11 to 6.90)	3.42 (0.52 to 22.53)	0.99 (0.14 to 7.23)	2.38 (0.53 to 10.69)
33.06 (0.64 to 1697.93)	5.47 (0.21 to 142.85)	12.57 (0.55 to 286.49)	16.11 (0.25 to 1052.41)	15.10 (0.74 to 306.72)	14.80 (0.65 to 339.06)	**23.35 (1.27 to 428.81)**	**24.73 (1.41 to 432.65)**	**42.36 (2.62 to 685.90)**	5.05 (0.38 to 67.51)	16.14 (0.88 to 294.52)	**21.72 (1.18 to 401.12)**	**17.47 (1.20 to 253.44)**	IT	1.08 (0.15 to 7.77)	0.35 (0.10 to 1.29)	0.46 (0.05 to 4.23)	0.30 (0.03 to 2.82)	1.14 (0.14 to 9.37)	0.33 (0.04 to 2.98)	0.80 (0.14 to 4.67)
3.63 (0.14 to 95.89)	0.60 (0.05 to 6.73)	1.38 (0.15 to 12.86)	1.77 (0.05 to 62.18)	1.66 (0.21 to 13.06)	1.63 (0.17 to 15.21)	2.56 (0.37 to 17.67)	2.72 (0.49 to 14.99)	4.65 (0.89 to 24.45)	0.55 (0.09 to 3.32)	1.77 (0.26 to 11.94)	2.39 (0.35 to 16.50)	1.92 (0.29 to 12.56)	0.11 (0.01 to 2.34)	MBT	0.33 (0.07 to 1.44)	0.43 (0.09 to 2.12)	0.28 (0.05 to 1.44)	1.06 (0.25 to 4.49)	0.31 (0.06 to 1.48)	0.74 (0.31 to 1.78)
3.10 (0.14 to 70.43)	0.51 (0.06 to 4.67)	1.18 (0.16 to 8.74)	1.51 (0.05 to 46.25)	1.42 (0.23 to 8.73)	1.39 (0.19 to 10.37)	2.19 (0.42 to 11.36)	2.32 (0.49 to 11.02)	3.97 (0.97 to 16.30)	0.47 (0.18 to 1.26)	1.51 (0.30 to 7.76)	2.04 (0.39 to 10.67)	1.64 (0.50 to 5.33)	0.09 (0.01 to 1.03)	0.85 (0.13 to 5.70)	ST	1.31 (0.22 to 7.91)	0.85 (0.13 to 5.33)	3.25 (0.62 to 17.04)	0.95 (0.16 to 5.54)	2.27 (0.68 to 7.53)
0.94 (0.06 to 15.27)	**0.15 (0.03 to 0.84)**	0.36 (0.09 to 1.43)	0.46 (0.02 to 10.34)	0.43 (0.15 to 1.22)	0.42 (0.14 to 1.24)	0.66 (0.11 to 3.97)	0.70 (0.11 to 4.45)	1.20 (0.25 to 5.81)	0.14 (0.02 to 1.07)	0.46 (0.08 to 2.76)	0.61 (0.10 to 3.75)	0.49 (0.08 to 3.18)	**0.03 (0.00 to 0.65)**	0.26 (0.03 to 2.42)	0.30 (0.04 to 2.27)	SSRIs+CBT	0.64 (0.35 to 1.17)	**2.47 (1.15 to 5.31)**	0.72 (0.44 to 1.19)	1.73 (0.45 to 6.57)
1.48 (0.08 to 26.47)	0.25 (0.04 to 1.54)	0.56 (0.12 to 2.67)	0.72 (0.03 to 17.76)	0.68 (0.19 to 2.36)	0.66 (0.19 to 2.26)	1.05 (0.15 to 7.38)	1.11 (0.15 to 8.26)	1.90 (0.33 to 11.10)	0.23 (0.03 to 1.96)	0.72 (0.10 to 5.14)	0.97 (0.14 to 6.96)	0.78 (0.10 to 5.89)	0.04 (0.00 to 1.14)	0.41 (0.04 to 4.39)	0.48 (0.05 to 4.17)	1.59 (0.48 to 5.25)	VEN+CBT	**3.84 (1.62 to 9.11)**	1.12 (0.60 to 2.09)	2.68 (0.66 to 10.84)
1.26 (0.07 to 21.30)	0.21 (0.04 to 1.22)	0.48 (0.11 to 2.15)	0.61 (0.03 to 14.38)	0.57 (0.17 to 1.99)	0.56 (0.12 to 2.57)	0.89 (0.35 to 2.26)	0.94 (0.32 to 2.78)	1.61 (0.84 to 3.11)	**0.19 (0.05 to 0.74)**	0.61 (0.25 to 1.51)	0.83 (0.32 to 2.13)	0.67 (0.23 to 1.95)	**0.04 (0.00 to 0.60)**	0.35 (0.06 to 1.88)	0.41 (0.10 to 1.57)	1.34 (0.29 to 6.22)	0.85 (0.15 to 4.71)	NT	**0.29 (0.15 to 0.58)**	0.70 (0.22 to 2.19)
4.04 (0.32 to 50.55)	0.67 (0.19 to 2.36)	1.54 (0.62 to 3.83)	1.97 (0.11 to 35.28)	1.84 (0.95 to 3.57)	1.81 (0.59 to 5.51)	2.85 (0.59 to 13.88)	3.02 (0.58 to 15.81)	**5.18 (1.33 to 20.16)**	0.62 (0.10 to 3.87)	1.97 (0.40 to 9.67)	2.65 (0.54 to 13.14)	2.13 (0.40 to 11.27)	0.12 (0.01 to 2.52)	1.11 (0.14 to 8.96)	1.30 (0.21 to 8.22)	**4.32 (1.31 to 14.19)**	2.72 (0.68 to 10.89)	3.21 (0.89 to 11.52)	PBO	2.40 (0.65 to 8.79)
0.94 (0.05 to 18.55)	0.16 (0.02 to 1.15)	0.36 (0.06 to 2.12)	0.46 (0.02 to 12.34)	0.43 (0.09 to 2.05)	0.42 (0.07 to 2.50)	0.66 (0.17 to 2.64)	0.70 (0.25 to 2.01)	1.20 (0.46 to 3.17)	**0.14 (0.04 to 0.47)**	0.46 (0.12 to 1.77)	0.62 (0.15 to 2.47)	0.50 (0.13 to 1.84)	**0.03 (0.00 to 0.44)**	0.26 (0.07 to 1.00)	0.30 (0.08 to 1.15)	1.00 (0.17 to 6.01)	0.63 (0.09 to 4.47)	0.75 (0.27 to 2.06)	0.23 (0.05 to 1.14)	TAU

Efficacy (frequency of nonsuicidal self-injury after treatment, OR [95%CI])
Acceptability (all-cause discontinuation, OR [95%CI])
Pharmacotherapy
Psychotherapy
Combination intervention
Control condition

Fig. 2 Network meta-analysis of efficacy and acceptability. Interventions were divided into four groups (pharmacotherapy, psychotherapy, combination intervention, and control condition) and each group was reported in alphabetical order. Comparisons between treatments are read from left to right, and the estimate is in cells in common between the column-defining treatment and the row-defining treatment. For efficacy (light brown) and acceptability (cyan), an odds ratio (OR) less than 1 favors the row-defining treatment. To obtain ORs for comparisons in the opposing direction, reciprocals should be taken. Significant results are in bold

rating scales to measure NSSI; in using rating scales, the C-SSRS seemed to be more sensitive for measuring NSSI than other scales (Fig. 4).

Concerning acceptability, in psychiatric disorders, patients with self-harm were associated with significantly fewer NSSI discontinuations (OR = 0.57; 95% CI:

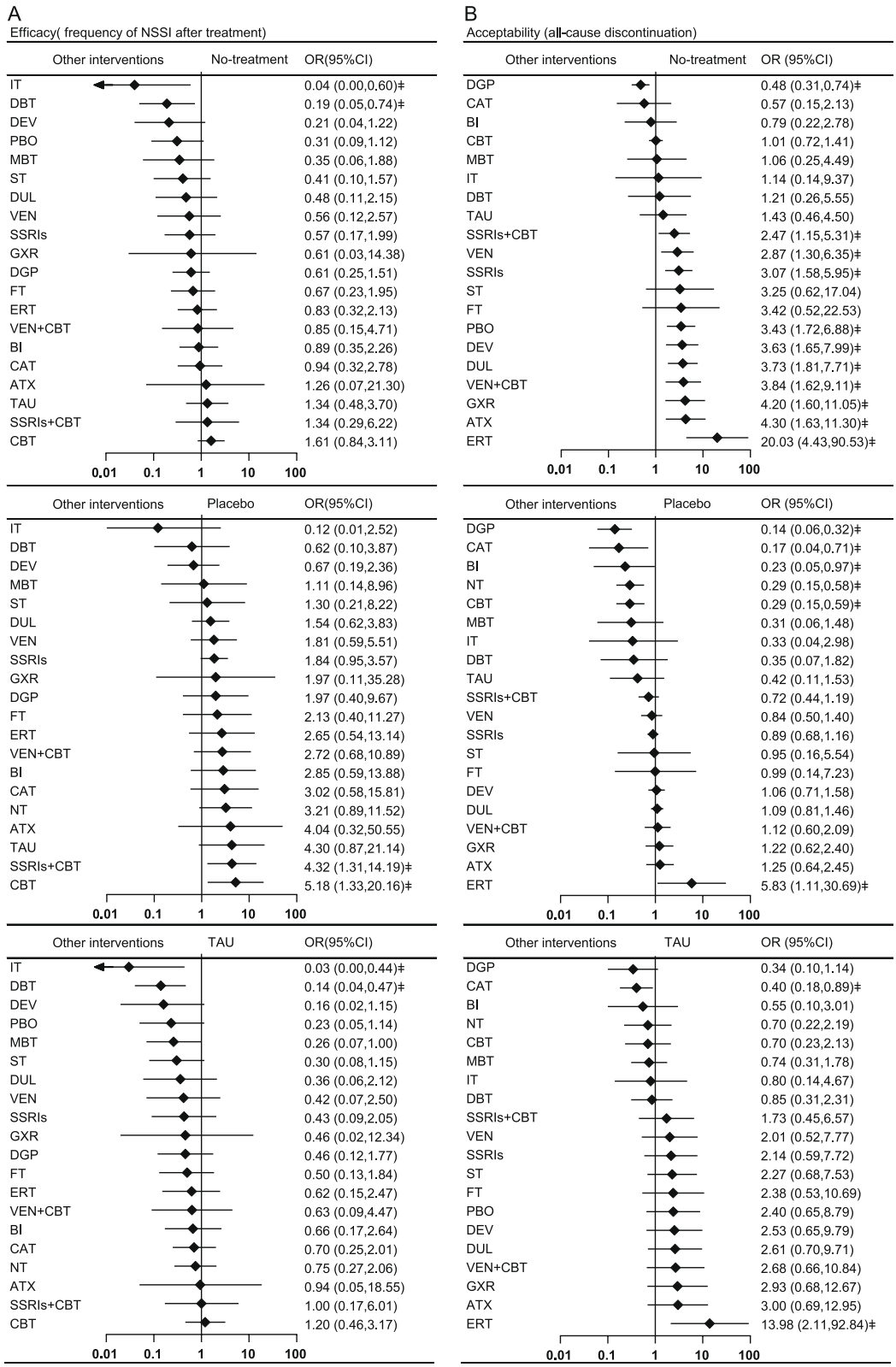
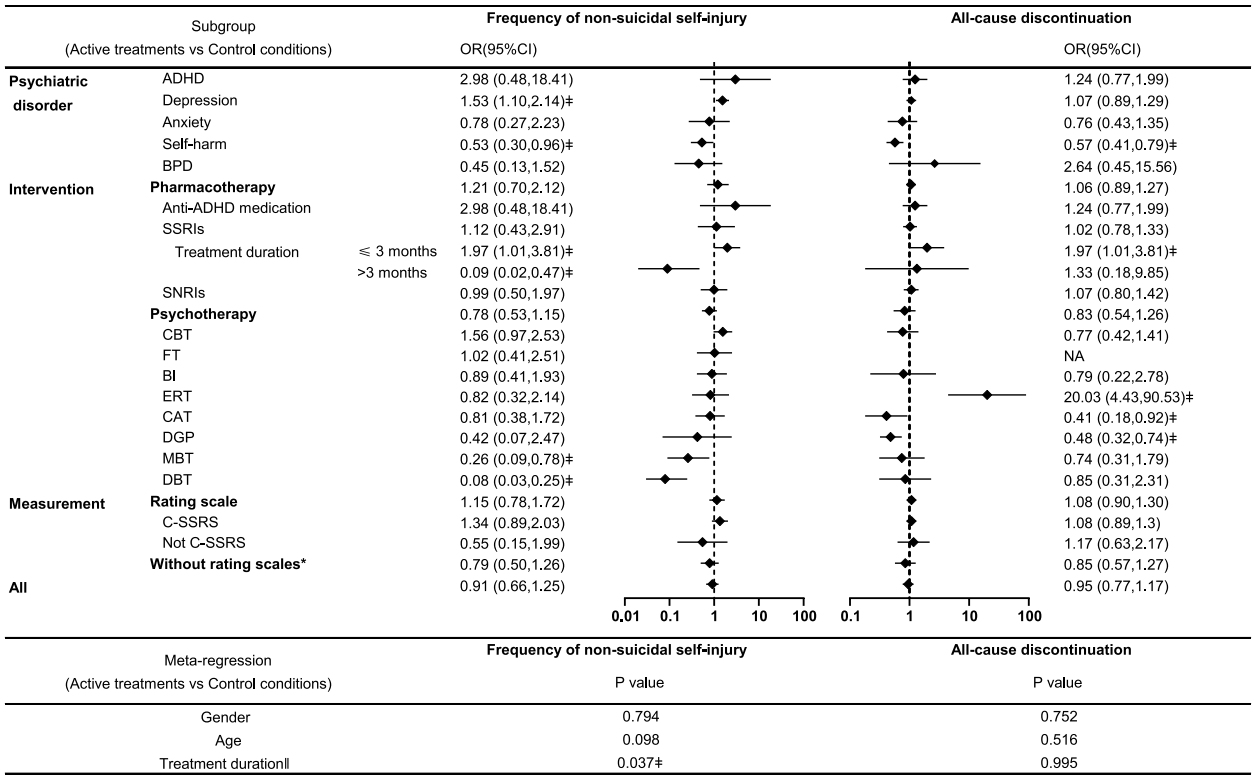


Fig. 3 Forest plots of network meta-analysis. **A** Efficacy. B Acceptability. Interventions were compared with placebo for efficacy and acceptability. Effect sizes represent summary odds ratios with 95% confidence intervals in network meta-analysis



Meta-regression (Active treatments vs Control conditions)	Frequency of non-suicidal self-injury P value	All-cause discontinuation P value
Gender	0.794	0.752
Age	0.098	0.516
Treatment duration‖	0.037‡	0.995

Fig. 4 Forest plots of subgroup analysis and results of meta-regression analysis. ADHD = Attention-deficit/hyperactivity disorder, BI = Brief intervention, BPD = Borderline personality disorder, CAT = Cognitive analytic therapy, CBT = Cognitive behavioral therapy, C-SSRS = Columbia–Suicide Severity Rating Scale, DBT = Dialectical behavior therapy, DGP = Developmental group psychotherapy, ERT = Emotion regulation training, FT = Family therapy, MBT = Mentalization-based treatment, SNRIs = Serotonin norepinephrine reuptake inhibitors, SSRIs = Selective serotonin reuptake inhibitors, *Using less strict assessment instruments (clinical interview or self-report). ‡ Significant results. ‖ Meta-regression analysis only conducted for comparisons of patients receiving selective serotonin reuptake inhibitor treatment

0.41 to 0.79; Fig. 4). There were significantly more discontinuations in the first 3 months when using SSRIs. CAT and DGP showed fewer NSSI discontinuations (ORs 0.41 and 0.48, respectively) whereas ERT showed significantly more discontinuations (OR = 20.03; 95% CI: 4.43 to 90.53; Fig. 4). Meta-regression analysis showed that sex and mean age did not significantly affect the efficacy and acceptability of interventions (Fig. 4).

Risk of bias and confidence of evidence assessment

According to CINeMA, 1 (1.8%) of the 57 comparisons for efficacy outcomes was rated as having a high confidence of evidence, 4 (7.0%) as moderate, 34 (59.6%) as low, and 18 (31.6%) were rated as very low confidence of evidence (Appendixes 4, 12). For the acceptability outcomes, 14 (24.6%) were rated as high confidence of evidence, 5 (8.8%) as moderate, 33 (57.9%) as low, and 5 (8.8%) as very low (Appendixes 4, 12).

Discussion

This systematic review and NMA for NSSI in children and adolescents included data from 28 RCTs including 6496 patients who were randomized to 19 active interventions or three control conditions. To our knowledge, this is the first study to compare pharmacotherapies, psychotherapies, and their combination in children and adolescents with NSSI using an NMA, thereby providing comprehensive and hierarchical evidence to help clinicians choose treatments to reduce the frequency of NSSI in children and adolescents with comorbid psychiatric disorders.

Similar to previous studies [19, 71], we found that DBT leads to more efficacious reductions in the frequency of NSSI than other treatments, especially TAU, with high confidence of evidence. On the contrary, as the basis of DBT, CBT was less efficacious than other treatments and even showed a worse tendency in NSSI. One reason for this is the differences in treatment structure between CBT and DBT. DBT is a comprehensive CBT method

[55], which was originally developed for chronically suicidal female patients who met the criteria for BPD [56]. Because the treatment developer did not find the standard CBT program to be successful to treat women with chronic suicidality, the treatment was amended to incorporate acceptance strategies grounded in Zen mindfulness to balance the change strategies emphasized in CBT treatment. Finally, DBT was developed based on the balance, flexibility, and synthesis of acceptance and change strategies in the delivery of treatment. We speculate that the role of Zen mindfulness to balance change strategies may be key to reducing suicidal behavior and NSSI. In addition, previous studies have shown that CBT should be considered a potential source of symptoms/adverse events [33] and CBT treatment for adolescents with both SI [5, 21, 73] and NSSI [5, 91] is associated with worse outcomes. The association of CBT with the onset of NSSI was probably due to increased contact and monitoring and contextual and behavioral functions of non-suicidal adverse events were not emphasized in this treatment model [13].

The United States has issued public health warnings regarding antidepressants, including SSRIs, which carry a risk of suicidal thoughts and behaviors in children and adolescents, based on the results of clinical trials [83]. One study describing suicidal tendencies in children and adolescents treated with SSRIs found that suicide-related behaviors and self-injury-related behaviors occurred primarily during the first three months of SSRI treatment [24]. Similar to previous results for SSI, we found that the frequency of NSSI was significantly increased in the first 3 months when using SSRIs for treatment and significantly reduced after 3 months. In addition, an observational study found that the number of NSSI events increased after SSRI initiation, although this finding was statistically non-significant [81]. However, owing to limited studies on the efficacy of SSRIs on NSSI, more high-quality clinical evidence is needed.

Compared with other psychiatric disorders, we found that patients with depression had a greater frequency of NSSI in subgroup analysis. Several studies also suggested that depressive symptoms may play a critical role in the development and persistence of NSSI [17, 48, 58, 87, 90, 95]), which is consistent with our results. We speculate that one reason for this is that NSSI is carried out to regulate depression. The experiential avoidance model [16] indicates that an individual may resort to self-injury when experiencing depression, which is an efficient method of regulating and combating depressive feelings [65],Tang WC, 2022). Moreover, compared with other mental diseases, patients with depression use more SSRIs, which leads to greater NSSI frequency. In addition, subgroup analysis showed that patients who experienced self-harm had less NSSI frequency. This may be because patients with self-harm were receiving treatments that are especially designed to target self-harm. However, there is no relevant evidence to support this, and further research is needed.

Previous meta-analyses about SSRIs and tricyclic antidepressant trials have shown that systematic assessment leads to higher rates of adverse events than less systematic assessment [72]. However, we did not find significant differences regarding whether to use rating scales to measure NSSI. Considering the influence of expectations, investigators likely expected substantial differences between the frequency of NSSI with active treatments and the control condition, which can substantially influence the outcome of experimental investigations [72, 74]. This expectation will be more significant in our results because it is difficult to double-blind investigators in psychotherapy studies. Regression analysis showed that sex and mean age did not significantly affect the efficacy and acceptability of interventions, but the treatment duration when using SSRIs for therapy significantly affected the efficacy and acceptability of interventions. Some studies indicated a potential correlation between NSSI or suicidal behavior in adolescents and sleep disturbances [9, 61]. However, further research is necessary to substantiate these findings.

Some interventions necessitate specialized training to be effectively implemented. However, future research should investigate strategies to incorporate low-intensity interventions or digital tools that require minimal clinician training. This would enhance accessibility for everyday practice. While certain interventions, such as "I Am Sober," have demonstrated potential in clinical settings, they have not yet been systematically evaluated within the NMA framework. Therefore, future research should rigorously examine their effectiveness through well-designed trials to expand the evidence base.

The study had several strengths. First, we included the age group ≤ 25 years, which has a high incidence of NSSI, and did not limit the country and region, which is likely to reasonably represent help-seeking young people with NSSI, making the results more broadly generalizable. Second, the definition of NSSI, the inclusion of intervention measures, the assessment of outcomes, and other aspects followed the PICO principle, and the selection of appropriate RCTs as data sources enhanced the accuracy and credibility of our results. Third, we compared and ranked efficacy and acceptability of psychotherapeutic, pharmacological, and combination treatments for NSSI in children and adolescents using NMA and conducted subgroup analysis of psychiatric disorders to provide evidence for clinicians to choose effective and safe treatments for patients with different psychiatric disorders.

Limitations

This study has several limitations. First, according to CINeMA assessment, the quality of most comparisons was low; many studies did not report adequate information. Second, we did not use the same measurements when counting NSSI outcomes. Because of the difficulty of double-blinding in some studies, using unstructured approaches may be influenced by the expectations of investigators, which may influence the results. Third, the lack of baseline frequency of NSSI in most included studies is a limitation that may affect the interpretation of treatment efficacy. Future studies should prioritize reporting both baseline and post-treatment NSSI frequency to allow for a more accurate assessment of treatment effects. Finally, a small number of studies compared the same treatments, which may make the results unstable; we cannot ensure that treatment efficacy will be same in the real world, meaning that the results should be interpreted with caution.

Conclusion

The findings of this NMA represent the most comprehensive analysis of the available evidence. As a mediator, depression seems to have a critical role in the development and persistence of NSSI. Moreover, NSSI is frequently used to combat depression symptoms, which may suggest that clinicians should give more attention to depression symptoms to reduce NSSI, especially in the first 3 months of SSRI treatment. The results of this review suggest that some psychotherapies have some efficacy for specific measures of NSSI, especially DBT. Based on the existing research, DBT may be considered the most effective option for reducing the frequency of NSSI. However, in recent years, given the increase in NSSI among adolescents, interventions are being specifically developed for NSSI management, and the study of interventions has been the focus of empirical research. Further verification in high-quality RCTs is still needed in the future.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-06735-1.

Supplementary Material 1

Acknowledgements
We thank LetPub (www.letpub.com) for its linguistic assistance during the preparation of this manuscript.

Clinical trial number
Not applicable. Our study is not a clinical trial, it is a system review and meta-analysis. We described in the study protocol registered a priori at PROSPERO (CRD42024510039).

Authors' contributions
X.C. wrote the protocol, managed the literature searches, analyzed data, and wrote the draft of the manuscript. Z.L. and C.Q. designed the study, wrote the protocol, and revised the manuscript. X.C. M.Y., and X.W. managed the literature searches and analyses. Data extraction was done by X.C and X.W; M.Y., and Y.Y. undertook the statistical analysis. J.Y. and X.C. also conducted the risk of bias assessment independently. L.G., Z.L, and C.Q. modified the manuscript. All authors contributed to and have approved the final manuscript.

Funding
This work was funded by the Zhejiang Medical Health Science and Technology Project (No. 2024KY484), the Shaoxing Medical Health Science and Technology Project (No. 2023SKY073), the Shaoxing Science and Technology Project (No. 2023A14030) and Shaoxing University enterprise important horizontal topic (No. 2024USXH287).

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable. All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

Consent to participate
Not applicable.

Competing interest
The authors declare no competing interests.

Author details
[1]Department of Psychiatry, Shaoxing Seventh People'S Hospital (Affiliated Mental Health Center of Shaoxing University), Shaoxing, Zhejiang, China. [2]Department of Behavioral Neurosciences, Science Research Center of Medical School, Shaoxing University, Shaoxing, Zhejiang, China. [3]Department of Blood Transfusion, Affiliated Hospital of Shaoxing University, Shaoxing, Zhejiang, China. [4]The Fifth People's Hospital of Zhuji, Shaoxing, Zhejiang, China.

Received: 20 September 2024 Accepted: 18 March 2025
Published online: 03 April 2025

References:

1. Andover MS, Schatten HT, Holman CS, Miller IW, Davila J. Moderators of treatment response to an intervention for nonsuicidal self-injury in young adults. J Consult Clin Psychol. 2020;88(11):1032–8. https://doi.org/10.1037/ccp0000603.
2. Andover MS, Schatten HT, Morris BW, Holman CS, Miller IW. An intervention for non-suicidal self-injury in young adults: a pilot randomized controlled trial. J Consult Clin Psychol. 2017;85(6):620–31. https://doi.org/10.1037/ccp0000206.
3. Andover MS, Schatten HT, Morris BW, Miller IW. Development of an intervention for nonsuicidal self-injury in young adults: an open pilot trial [Journal Article]. Cogn Behav Pract. 2015;22(4):491–503. https://doi.org/10.1016/j.cbpra.2014.05.003.
4. Andover MS, Gibb BE. Non-suicidal self-injury, attempted suicide, and suicidal intent among psychiatric inpatients. Psychiatry Res. 2010;178(1):101–5. https://doi.org/10.1016/j.psychres.2010.03.019.
5. Asarnow JR, Emslie G, Clarke G, Wagner KD, Spirito A, Vitiello B, Iyengar S, Shamseddeen W, Ritz L, Birmaher B, Ryan N, Kennard B, Mayes T, DeBar L, McCracken J, Strober M, Suddath R, Leonard H, Porta G, Keller M, Brent D. Treatment of selective serotonin reuptake inhibitor-resistant depression in adolescents: predictors and moderators of treatment response [Comparative Study; Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, N.I.H., Extramural]. J Am Acad Child Adolesc Psychiatry. 2009;48(3):330–9. https://doi.org/10.1097/chi.0b013e3181977476.

6. Asarnow JR, Porta G, Spirito A, Emslie G, Clarke G, Wagner KD, Vitiello B, Keller M, Birmaher B, McCracken J, Mayes T, Berk M, Brent DA. Suicide attempts and nonsuicidal self-injury in the treatment of resistant depression in adolescents: findings from the TORDIA study [Journal Article; Randomized Controlled Trial; Research Support, N.I.H., Extramural]. J Am Acad Child Adolesc Psychiatry. 2011;50(8):772–81. https://doi.org/10.1016/j.jaac.2011.04.003.
7. Atkinson S, et al. Desvenlafaxine versus placebo in the treatment of children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2018;28(1):55–65. https://doi.org/10.1089/cap.2017.0099.
8. Atkinson SD, et al. A double-blind efficacy and safety study of duloxetine flexible dosing in children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2014;24(4):180–9. https://doi.org/10.1089/cap.2013.0146.
9. Baldini V, Gnazzo M, Rapelli G, Marchi M, Pingani L, Ferrari S, De Ronchi D, Varallo G, Starace F, Franceschini C, Musetti A, Poletti M, Ostuzzi G, Pizza F, Galeazzi GM, Plazzi G. Association between sleep disturbances and suicidal behavior in adolescents: a systematic review and meta-analysis. Front Psych. 2024;15: 1341686. https://doi.org/10.3389/fpsyt.2024.1341686.
10. Bjureberg J, Ojala O, Hesser H, Habel H, Sahlin H, Gratz KL, Tull MT, Claesdotter KE, Hedman-Lagerlof E, Ljotsson B, Hellner C. Effect of internet-delivered emotion regulation individual therapy for adolescents with nonsuicidal self-injury disorder: a randomized clinical trial [Journal Article; Randomized Controlled Trial]. JAMA Netw Open. 2023;6(7):e2322069. https://doi.org/10.1001/jamanetworkopen.2023.22069.
11. Bjureberg J, Sahlin H, Hedman-Lagerlof E, Gratz KL, Tull MT, Jokinen J, Hellner C, Ljotsson B. Extending research on Emotion Regulation Individual Therapy for Adolescents (ERITA) with nonsuicidal self-injury disorder: open pilot trial and mediation analysis of a novel online version [Clinical Trial; Journal Article; Research Support, Non-U.S. Gov't]. BMC Psychiatry. 2018;18(1):326. https://doi.org/10.1186/s12888-018-1885-6.
12. Bjureberg J, Sahlin H, Hellner C, Hedman-Lagerlof E, Gratz KL, Bjarehed J, Jokinen J, Tull MT, Ljotsson B. Emotion regulation individual therapy for adolescents with nonsuicidal self-injury disorder: a feasibility study [Clinical Trial; Journal Article; Research Support, Non-U.S. Gov't]. BMC Psychiatry. 2017;17(1):411. https://doi.org/10.1186/s12888-017-1527-4.
13. Brent DA, Emslie GJ, Clarke GN, Asarnow J, Spirito A, Ritz L, Vitiello B, Iyengar S, Birmaher B, Ryan ND, Zelazny J, Onorato M, Kennard B, Mayes TL, Debar LL, McCracken JT, Strober M, Suddath R, Leonard H, Porta G, Keller MB. Predictors of spontaneous and systematically assessed suicidal adverse events in the treatment of SSRI-resistant depression in adolescents (TORDIA) study [Journal Article; Multicenter Study; Randomized Controlled Trial]. Am J Psychiatry. 2009;166(4):418–26. https://doi.org/10.1176/appi.ajp.2008.08070976.
14. Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G, Haibe-Kains B. Graphical tools for network meta-analysis in STATA. PLoS ONE. 2013;8(10): e76654. https://doi.org/10.1371/journal.pone.0076654.
15. Chanen AM, et al. Early intervention for adolescents with borderline personality disorder using cognitive analytic therapy: randomised controlled trial. Br J Psychiatr. 2008;193(6):477–84. https://doi.org/10.1192/bjp.bp.107.048934.
16. Chapman AL, Gratz KL, Brown MZ. Solving the puzzle of deliberate self-harm: the experiential avoidance model [Journal Article; Review]. Behav Res Ther. 2006;44(3):371–94. https://doi.org/10.1016/j.brat.2005.03.005.
17. Cipriano A, Cella S, Cotrufo P. Nonsuicidal self-injury: a systematic review. Front Psychol. 2017;8(8):1946–59. https://doi.org/10.3389/fpsyg.2017.01946. eCollection 2017 .
18. Cloutier P, Martin J, Kennedy A, Nixon MK, Muehlenkamp JJ. Characteristics and co-occurrence of adolescent non-suicidal self-injury and suicidal behaviours in pediatric emergency crisis services [Journal Article; Research Support, Non-U.S. Gov't]. J Youth Adolesc. 2010;39(3):259–69. https://doi.org/10.1007/s10964-009-9465-1.
19. Cook NE, Gorraiz M. Dialectical behavior therapy for nonsuicidal self-injury and depression among adolescents: preliminary meta-analytic evidence [Journal Article]. Child Adolesc Ment Health. 2016;21(2):81–9. https://doi.org/10.1111/camh.12112.
20. Cotgrove A, et al. Secondary prevention of attempted suicide in adolescence. J Adolesc (London, England.). 1995;18(5):569–77.
21. Curry J, Rohde P, Simons A, Silva S, Vitiello B, Kratochvil C, Reinecke M, Feeny N, Wells K, Pathak S, Weller E, Rosenberg D, Kennard B, Robins M, Ginsburg G, March J. Predictors and moderators of acute outcome in the Treatment for Adolescents with Depression Study (TADS) [Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't]. J Am Acad Child Adolesc Psychiatry. 2006;45(12):1427–39. https://doi.org/10.1097/01.chi.0000240838.78984.e2.
22. Davey CG, et al. The addition of fluoxetine to cognitive behavioural therapy for youth depression (YoDA-C): a randomised, double-blind, placebo-controlled, multicentre clinical trial. Lancet Psychiatr. 2019;6(9):735–44. https://doi.org/10.1016/S2215-0366(19)30215-9.
23. Diamond GS, et al. A Randomized-Controlled Trial: Attachment-Based Family and Non-Directive Supportive Treatments for Suicidal Youth. J Am Acad Child Adolesc Psychiatr. 2019;58(7):721–31. https://doi.org/10.1016/j.jaac.2018.10.006.
24. Dubrall D, Fekete S, Leitzen S, Paschke LM, Romanos M, Schmid M, Gerlach M, Sachs B. Selective serotonin reuptake inhibitors and suicidality in children and young adults: analyses of pharmacovigilance databases. BMC Pharmacol Toxicol. 2023;24(1):22. https://doi.org/10.1186/s40360-023-00664-z.
25. Dulit RA, Fyer MR, Leon AC, Brodsky BS, Frances AJ. Clinical correlates of self-mutilation in borderline personality disorder [Journal Article; Research Support, Non-U.S. Gov't]. American J Psychiatry. 1994;151(9):1305–11. https://doi.org/10.1176/ajp.151.9.1305.
26. Edinger A, Fischer-Waldschmidt G, Parzer P, Brunner R, Resch F, Kaess M. The impact of adverse childhood experiences on therapy outcome in adolescents engaging in nonsuicidal self-injury. Front Psych. 2020;11: 505661. https://doi.org/10.3389/fpsyt.2020.505661.
27. Eggart V, Cordier S, Hasan A, Wagner E. Psychotropic drugs for the treatment of non-suicidal self-injury in children and adolescents: a systematic review and meta-analysis. Eur Arch Psychiatry Clin Neurosci. 2022;272(8):1559–68. https://doi.org/10.1007/s00406-022-01385-w.
28. Emslie GJ, et al. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. J Am Acad Child Adolesc Psychiatr. 2009;48(7):721–29. https://doi.org/10.1097/CHI.0b013e3181a2b304.
29. Emslie GJ, et al. A double-blind efficacy and safety study of duloxetine fixed doses in children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2014;24(4)170–79. https://doi.org/10.1089/cap.2013.0096.
30. Esposito Smythers C, et al. Family-focused cognitive behavioral treatment for depressed adolescents in suicidal crisis with co-occurring risk factors: a randomized trial. J Child Psychol Psychiatr. 2019;60(10):1133–41. https://doi.org/10.1111/jcpp.13095.
31. Favazza AR, Conterio K. Female habitual self-mutilators [Journal Article]. Acta Psychiatr Scand. 1989;79(3):283–9. https://doi.org/10.1111/j.1600-0447.1989.tb10259.x.
32. Fischer G, Brunner R, Parzer P, Resch F, Kaess M. Short-term psychotherapeutic treatment in adolescents engaging in non-suicidal self-injury: a randomized controlled trial [Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. Trials. 2013;14:294. https://doi.org/10.1186/1745-6215-14-294.
33. Foa EB, Zoellner LA, Feeny NC, Hembree EA, Alvarez-Conrad J. Does imaginal exposure exacerbate PTSD symptoms? [Journal Article; Research Support, U.S. Gov't, P.H.S.]. J Consult Clin Psychol. 2002;70(4):1022–8. https://doi.org/10.1037/0022-006x.70.4.1022.
34. Fox KR, Millner AJ, Franklin JC. Classifying nonsuicidal overdoses: nonsuicidal self-injury, suicide attempts, or neither? Psychiatry Res. 2016;244:235–42. https://doi.org/10.1016/j.psychres.2016.07.052.
35. Goodyer I, Dubicka B, Wilkinson P, Kelvin R, Roberts C, Byford S, Breen S, Ford C, Barrett B, Leech A, Rothwell J, White L, Harrington R. Selective serotonin reuptake inhibitors (SSRIs) and routine specialist care with and without cognitive behaviour therapy in adolescents with major depression: randomised controlled trial [Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. BMJ. 2007;335(7611):142. https://doi.org/10.1136/bmj.39224.494340.55.
36. Grandclerc S, De Labrouhe D, Spodenkiewicz M, Lachal J, Moro M, Botbol M. Relations between nonsuicidal self-injury and suicidal behavior in adolescence: a systematic review. PLoS ONE. 2016;11(4): e153760. https://doi.org/10.1371/journal.pone.0153760.

37. Green JM, Wood AJ, Kerfoot MJ, Trainor G, Roberts C, Rothwell J, Woodham A, Ayodeji E, Barrett B, Byford S, Harrington R. Group therapy for adolescents with repeated self harm: randomised controlled trial with economic evaluation [Journal Article; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. BMJ. 2011;342:d682. https://doi.org/10.1136/bmj.d682.
38. Guan K, Fox KR, Prinstein MJ. Nonsuicidal self-injury as a time-invariant predictor of adolescent suicide ideation and attempts in a diverse community sample. J Consult Clin Psychol. 2012;80(5):842.
39. Harrington R, et al. Randomized trial of a home-based family intervention for children who Have deliberately poisoned themselves. J Am Acad Child Adolesc Psychiatr. 1998;37(5):512–8.
40. Hawton K, Bergen H, Cooper J, Turnbull P, Waters K, Ness J, Kapur N. Suicide following self-harm: findings from the Multicentre Study of self-harm in England, 2000–2012 [Journal Article; Multicenter Study; Research Support, Non-U.S. Gov't]. J Affect Disord. 2015;175:147–51. https://doi.org/10.1016/j.jad.2014.12.062.
41. Hervas A. et al., Efficacy and safety of extended-release guanfacine hydrochloride in children and adolescents with attention-deficit/hyperactivity disorder: A randomized, controlled, Phase III trial. Eur Neuropsychopharmacol. 2014;24(12):1861–72. https://doi.org/10.1016/j.euroneuro.2014.09.014.
42. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557.
43. Higgins JP, Jackson D, Barrett JK, Lu G, Ades AE, White IR. Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies [Journal Article]. Res Synth Methods. 2012;3(2):98–110. https://doi.org/10.1002/jrsm.1044.
44. Hurtado-Santiago S, et al. Iconic therapy for the reduction of borderline personality disorder symptoms among suicidal youth: a preliminary study. BMC Psychiatr. 2022;22(1):224. https://doi.org/10.1186/s12888-022-03862-x.
45. Iyengar U, Snowden N, Asarnow JR, Moran P, Tranah T, Ougrin D. A further look at therapeutic interventions for suicide attempts and self-harm in adolescents: an updated systematic review of randomized controlled trials. Front Psych. 2018;9: 583. https://doi.org/10.3389/fpsyt.2018.00583.
46. Jackson D, Riley RD. A refined method for multivariate meta-analysis and meta-regression [Journal Article; Research Support, Non-U.S. Gov't]. Stat Med. 2014;33(4):541–54. https://doi.org/10.1002/sim.5957.
47. Jacobson CM, Muehlenkamp JJ, Miller AL, Turner JB. Psychiatric impairment among adolescents engaging in different types of deliberate self-harm [Journal Article]. J Clin Child Adolesc Psychol. 2008;37(2):363–75. https://doi.org/10.1080/15374410801955771.
48. Jiang Y, Ren Y, Liu T, You J. Rejection sensitivity and adolescent nonsuicidal self-injury: Mediation through depressive symptoms and moderation by fear of self-compassion [Journal Article; Research Support, Non-U.S. Gov't]. Psychol Psychother. 2021;94(Suppl 2):481–96. https://doi.org/10.1111/papt.12293.
49. Joan Rosenbaum Asarnow LM. (2019). Practitioner review: treatment for suicidal and selfharming adolescents – advances in suicide prevention care. J Child Psychol Psychiatr. 2019;60(10):1046–54. https://doi.org/10.1111/jcpp.13130.
50. Kaess M, Edinger A, Fischer-Waldschmidt G, Parzer P, Brunner R, Resch F. Effectiveness of a brief psychotherapeutic intervention compared with treatment as usual for adolescent nonsuicidal self-injury: a single-centre, randomised controlled trial [Journal Article; Randomized Controlled Trial]. Eur Child Adolesc Psychiatry. 2020;29(6):881–91. https://doi.org/10.1007/s00787-019-01399-1.
51. Kennard BD, et al. As Safe as Possible (ASAP): a brief app-supported inpatient intervention to prevent postdischarge suicidal behavior in hospitalized, suicidal adolescents. Am J Psychiatr. 2018;175(9):864. https://doi.org/10.1176/appi.ajp.2018.17101151.
52. Power KG, Spencer AP. Parasuicidal behaviour of detained Scottish young offenders. Int J Offender Ther Comp Criminol. 1987.
53. Kiekens G, Hasking P, Bruffaerts R, Alonso J, Auerbach RP, Bantjes J, Benjet C, Boyes M, Chiu WT, Claes L, Cuijpers P, Ebert DD, Mak A, Mortier P, O'Neill S, Sampson NA, Stein DJ, Vilagut G, Nock MK, Kessler RC. Non-suicidal self-injury among first-year college students and its association with mental disorders: results from the World Mental Health International College Student (WMH-ICS) initiative [Journal Article; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't]. Psychol Med. 2023;53(3):875–86. https://doi.org/10.1017/S0033291721002245.
54. Klonsky ED, Muehlenkamp JJ. Self-injury: a research review for the practitioner [Comparative Study; Journal Article; Review]. J Clin Psychol. 2007;63(11):1045–56. https://doi.org/10.1002/jclp.20412.
55. Linehan MM. Cognitive-behavioral treatment of borderline personality disorder. Cognitive-behavioral treatment of borderline personality disorder. New York NY US. 1993;558:558 Guilford Press.
56. Linehan MM, Armstrong HE, Suarez A, Allmon D, Heard HL. Cognitive-behavioral treatment of chronically parasuicidal borderline patients [Clinical Trial; Comparative Study; Journal Article; Randomized Controlled Trial; Research Support, U.S. Gov't, P.H.S.]. Arch Gen Psychiatry. 1991;48(12):1060–4. https://doi.org/10.1001/archpsyc.1991.01810360024003.
57. Liu Y, Wang W, Zhang AB, Bai X, Zhang S. Epley and Semont maneuvers for posterior canal benign paroxysmal positional vertigo: A network meta-analysis [Journal Article; Meta-Analysis]. Laryngoscope. 2016;126(4):951–5. https://doi.org/10.1002/lary.25688.
58. Liu ZZ, Tein JY, Jia CX, Liu X. Depression as a mediator between frequent nightmares and non-suicidal self-injury among adolescents: a 3-wave longitudinal model [Journal Article; Research Support, Non-U.S. Gov't]. Sleep Med. 2021;77:29–34. https://doi.org/10.1016/j.sleep.2020.11.015.
59. Lloyd-Richardson EE, Perrine N, Dierker L, Kelley ML. Characteristics and functions of non-suicidal self-injury in a community sample of adolescents. Psychol Med. 2007;37(8):1183–92. https://doi.org/10.1017/S0033291707000027X.
60. McCauley E, et al. Efficacy of dialectical behavior therapy for adolescents at high risk for suicide. JAMA Psychiatr. 2018;75(8):777. https://doi.org/10.1001/jamapsychiatry.2018.1109.
61. McGlinchey EL, Courtney-Seidler EA, German M, Miller AL. (2017). The role of sleep disturbance in suicidal and nonsuicidal self-injurious behavior among adolescents. (47, pp. 103–111). United Kingdom: Wiley-Blackwell Publishing Ltd.
62. Mehlum L, Tormoen AJ, Ramberg M, Haga E, Diep LM, Laberg S, Larsson BS, Stanley BH, Miller AL, Sund AM, Groholt B. Dialectical behavior therapy for adolescents with repeated suicidal and self-harming behavior: a randomized trial [Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. J Am Acad Child Adolesc Psychiatry. 2014;53(10):1082–91. https://doi.org/10.1016/j.jaac.2014.07.003.
63. Melvin GA, et al. Adverse events reported by anxious school refusing adolescents receiving cognitive behavioral therapy with and without fluoxetine. Clinical Child Psychology and Psychiatr. 2019;24(4):892–905. https://doi.org/10.1177/1359104518822681.
64. Monto MA, McRee N, Deryck FS. Nonsuicidal Self-Injury Among a Representative Sample of US Adolescents, 2015. Am J Public Health. 2018;108(8):1042–8. https://doi.org/10.2105/AJPH.2018.304470.
65. Nock MK. Why do people hurt themselves? New insights into the nature and functions of self-injury [Journal Article]. Curr Dir Psychol Sci. 2009;18(2):78–83. https://doi.org/10.1111/j.1467-8721.2009.01613.x.
66. Nock MK, Prinstein MJ. A Functional Approach to the Assessment of Self-Mutilative Behavior. J Consult Clin Psychol. 2004;72(5):885–90. https://doi.org/10.1037/0022-006X.72.5.885.
67. Nock M, Joiner T Jr, Gordon K, Lloyd-Richardson E, Prinstein M. Non-suicidal self-injury among adolescents: Diagnostic correlates and relation to suicide attempts. Psychiatry Res. 2006;144(1):65–72. https://doi.org/10.1016/j.psychres.2006.05.010.
68. Ougrin D, Boege I, Stahl D, Banarsee R, Taylor E. Randomised controlled trial of therapeutic assessment versus usual assessment in adolescents with self-harm: 2-year follow-up [Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. Arch Dis Childh. 2013;98(10):772–6. https://doi.org/10.1136/archdischild-2012-303200.
69. Ougrin D, Tranah T, Stahl D, Moran P, Asarnow JR. Therapeutic interventions for suicide attempts and self-harm in adolescents: systematic review and meta-analysis [Journal Article; Meta-Analysis; Research Support, Non-U.S. Gov't; Review; Systematic Review]. J Am Acad Child Adolesc Psychiatry. 2015;54(2):97–107. https://doi.org/10.1016/j.jaac.2014.10.009.
70. Perez AV, Ibanez-Beroiz B, Goni-Sarries A, Galbete JA. Efficacy of psychotherapeutic interventions for non-suicidal self-injury in adolescent

population: systematic review and meta-analysis [Journal Article; Meta-Analysis; Review; Systematic Review]. Span J Psychiatry Ment Health. 2023;16(2):119–26. https://doi.org/10.1016/j.rpsm.2022.10.001.
71. Pistorello J, Fruzzetti AE, Maclane C, Gallop R, Iverson KM. Dialectical behavior therapy (DBT) applied to college students: a randomized clinical trial [Journal Article; Randomized Controlled Trial; Research Support, N.I.H., Extramural]. J Consult Clin Psychol. 2012;80(6):982–94. https://doi.org/10.1037/a0029096.
72. Rief W, Nestoriuc Y, von Lilienfeld-Toal A, Dogan I, Schreiber F, Hofmann SG, Barsky AJ, Avorn J. Differences in adverse effect reporting in placebo groups in SSRI and tricyclic antidepressant trials: a systematic review and meta-analysis [Journal Article; Meta-Analysis; Research Support, Non-U.S. Gov't; Review; Systematic Review]. Drug Saf. 2009;32(11):1041–56. https://doi.org/10.2165/11316580-000000000-00000.
73. Rohde P, Seeley JR, Kaufman NK, Clarke GN, Stice E. Predicting time to recovery among depressed adolescents treated in two psychosocial group interventions [Journal Article; Research Support, N.I.H., Extramural]. J Consult Clin Psychol. 2006;74(1):80–8. https://doi.org/10.1037/0022-006X.74.1.80.
74. Rosenthal R. Experimenter effects in behavioral research. New York and London: Irvington Publishers; 1976.
75. Rossouw TI, Fonagy P. Mentalization-based treatment for self-harm in adolescents: a randomized controlled trial. J Am Acad Child Adolesc Psychiatr. 2012;51(12):1304–13.e3. https://doi.org/10.1016/j.jaac.2012.09.018.
76. Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. PLoS One. 2014;9(7):e99682. https://doi.org/10.1371/journal.pone.0099682. eCollection 2014.
77. Santamarina Perez P, Mendez I, Singh MK, Berk M, Picado M, Font E, Moreno E, Martínez E, Morer A, Borràs R, Cosi A, Romero S. Adapted Dialectical Behavior Therapy for Adolescents with a High Risk of Suicide in a Community Clinic: A Pragmatic Randomized Controlled Trial. Suicide Life Threat Behav. 2020;50(3):652–67. https://doi.org/10.1111/sltb.12612.
78. Schuppert HM, et al, Effectiveness of an emotion regulation group training for adolescents--a randomized controlled pilot study. Clin Psychol Psychother. 2009;16(6):467–78. https://doi.org/10.1002/cpp.637.
79. Schuppert HM, et al. Emotion regulation training for adolescents with borderline personality disorder traits: a randomized controlled trial. J Am Acad Child Adolesc Psychiatr. 2012;51(12):1314–23.e2. https://doi.org/10.1016/j.jaac.2012.09.002.
80. Skegg K. Self-harm. Lancet. 2005;366(9495):1471–83. https://doi.org/10.1016/S0140-6736(05)67600-3.
81. Sorensen JO, Rasmussen A, Roesbjerg T, Verhulst FC, Pagsberg AK. Suicidality and self-injury with selective serotonin reuptake inhibitors in youth: Occurrence, predictors and timing [Journal Article; Observational Study]. Acta Psychiatr Scand. 2022;145(2):209–22. https://doi.org/10.1111/acps.13360.
82. Steinhoff A, Ribeaud D, Kupferschmid S, Raible-Destan N, Quednow BB, Hepp U, Eisner M, Shanahan L. Self-injury from early adolescence to early adulthood: age-related course, recurrence, and services use in males and females from the community [Journal Article]. Eur Child Adolesc Psychiatry. 2021;30(6):937–51. https://doi.org/10.1007/s00787-020-01573-w.
83. Stone M, Laughren T, Jones ML, Levenson M, Holland PC, Hughes A, Hammad TA, Temple R, Rochester G. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US food and drug administration [Journal Article; Meta-Analysis; Review]. BMJ. 2009;339:b2880. https://doi.org/10.1136/bmj.b2880.
84. Strawn JR, et al. A randomized, placebo-controlled study of duloxetine for the treatment of children and adolescents with generalized anxiety disorder. J Am Acad Child Adolesc Psychiatr. 2015;54(4):283–93. https://doi.org/10.1016/j.jaac.2015.01.008.
85. Swannell SV, Martin GE, Page A, Hasking P, St John NJ. Prevalence of nonsuicidal self-injury in nonclinical samples: systematic review, meta-analysis and meta-regression [Journal Article; Meta-Analysis; Review; Systematic Review]. Suicide Life Threat Behav. 2014;44(3):273–303. https://doi.org/10.1111/sltb.12070.
86. Sweeting MJ, Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data [Comparative Study; Journal Article; Research Support, Non-U.S. Gov't]. Stat Med. 2004;23(9):1351–75. https://doi.org/10.1002/sim.1761.
87. Tang WC, Lin MP, Wu JY. Mediating role of depression in the association between alexithymia and nonsuicidal self-injury in a representative sample of adolescents in Taiwan. Child Adolesc Psychiatry Ment Health. 2022;16(1):43.
88. Taylor LM, Oldershaw A, Richards C, Davidson K, Schmidt U, Simic M. Development and pilot evaluation of a manualized cognitive-behavioural treatment package for adolescent self-harm [Evaluation Study; Journal Article]. Behav Cogn Psychother. 2011;39(5):619–25. https://doi.org/10.1017/S1352465811000075.
89. Turner BJ, Austin SB, Chapman AL. Treating nonsuicidal self-injury: a systematic review of psychological and pharmacological interventions (59, pp. 576-585). Los Angeles, CA: SAGE Publications. 2014.
90. Valencia-Agudo F, Burcher GC, Ezpeleta L, Kramer T. Nonsuicidal self-injury in community adolescents: A systematic review of prospective predictors, mediators and moderators [Journal Article; Research Support, Non-U.S. Gov't; Systematic Review]. J Adolesc. 2018;65:25–38. https://doi.org/10.1016/j.adolescence.2018.02.012.
91. Victor SE, Muehlenkamp JJ, Hayes NA, Lengel GJ, Styer DM, Washburn JJ. Characterizing gender differences in nonsuicidal self-injury: Evidence from a large clinical sample of adolescents and adults. Compr Psychiatry. 2018;82:53–60.
92. Walkup JT, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. N Engl J Med. 2008;359(26). https://doi.org/10.1056/NEJMoa0804633.
93. Webb CA, et al. Which adolescents are well-suited to app-based mindfulness training? A randomized clinical trial and data-driven approach for personalized recommendations. J Consult Clin Psychol. 2022;90(9):655–69. https://doi.org/10.1037/ccp0000763.
94. Weihs KL, et al. Desvenlafaxine versus placebo in a fluoxetine-referenced study of children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2018;28(1):36–46. https://doi.org/10.1089/cap.2017.0100.3.
95. Wei C, Li J, Yu C, Chen Y, Zhen S, Zhang W. Deviant Peer Affiliation and Non-Suicidal Self-Injury among Chinese Adolescents: Depression as a Mediator and Sensation Seeking as a Moderator [Journal Article; Research Support, Non-U.S. Gov't]. Int J Environ Res Public Health. 2021;18(16):8355. https://doi.org/10.3390/ijerph18168355.
96. White IR, Barrett JK, Jackson D, Higgins JP. Consistency and inconsistency in network meta-analysis: model estimation using multivariate meta-regression [Journal Article]. Res Synth Methods. 2012;3(2):111–25. https://doi.org/10.1002/jrsm.1045.
97. Wilkinson P, Kelvin R, Roberts C, Dubicka B, Goodyer I. Clinical and psychosocial predictors of suicide attempts and nonsuicidal self-injury in the Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT) [Journal Article; Research Support, Non-U.S. Gov't]. Am J Psychiatry. 2011;168(5):495–501. https://doi.org/10.1176/appi.ajp.2010.10050718.
98. Wong J, Bahji A, Khalid-Khan S. Psychotherapies for Adolescents with Subclinical and Borderline Personality Disorder: A Systematic Review and Meta-Analysis [Journal Article; Meta-Analysis; Systematic Review]. Can J Psychiatry. 2020;65(1):5–15. https://doi.org/10.1177/0706743719878975.
99. Wood A, Trainor G, Rothwell J, Moore A, Harrington R. Randomized trial of group therapy for repeated deliberate self-harm in adolescents [Clinical Trial; Journal Article; Randomized Controlled Trial; Research Support, Non-U.S. Gov't]. J Am Acad Child Adolesc Psychiatry. 2001;40(11):1246–53. https://doi.org/10.1097/00004583-200111000-00003.
100. Zetterqvist M, Jonsson LS, Landberg Å, Svedin CG. A potential increase in adolescent nonsuicidal self-injury during covid-19: A comparison of data from three different time points during 2011–2021. Psychiatry Res. 2021;305: 114208. https://doi.org/10.1016/j.psychres.2021.114208.

Publisher's Note