Therapeutic Interventions for Suicide Attempts and Self-Harm in Adolescents: Systematic Review and Meta-Analysis

Dennis Ougrin, MBBS, MRCPsych, PGDip(Oxon), PhD, Troy Tranah, BSc, MSc, PhD, Daniel Stahl, PhD, Paul Moran, MBBS, BSc, MSc, DLSHTM, MD, MRCPsych, Joan Rosenbaum Asarnow, PhD

Objective: Suicidal behavior and self-harm are common in adolescents and are associated with elevated psychopathology, risk of suicide, and demand for clinical services. Despite recent advances in the understanding and treatment of self-harm and links between self-harm and suicide and risk of suicide attempt, progress in reducing suicide death rates has been elusive, with no substantive reduction in suicide death rates over the past 60 years. Extending prior reviews of the literature on treatments for suicidal behavior and repetitive self-harm in youth, this article provides a meta-analysis of randomized controlled trials (RCTs) reporting efficacy of specific pharmacological, social, or psychological therapeutic interventions (TIs) in reducing both suicidal and nonsuicidal self-harm in adolescents.

Method: Data sources were identified by searching the Cochrane, Medline, PsychINFO, EMBASE, and PubMed databases as of May 2014. RCTs comparing specific therapeutic interventions versus treatment as usual (TAU) or placebo in adolescents (through age 18 years) with self-harm were included.

Results: Nineteen RCTs including 2,176 youth were analyzed. TIs included psychological and social interventions and no pharmacological interventions. The proportion of the adolescents who self-harmed over the follow-up period was lower in the intervention groups (28%) than in controls (33%) (test for overall effect $z = 2.31$; $p = .02$). TIs with the largest effect sizes were dialectical behavior therapy (DBT), cognitive-behavioral therapy (CBT), and mentalization-based therapy (MBT). There were no independent replications of efficacy of any TI. The pooled risk difference between TIs and TAU for suicide attempts and nonsuicidal self-harm considered separately was not statistically significant.

Conclusion: TIs to prevent self-harm appear to be effective. Independent replication of the results achieved by DBT, MBT, and CBT is a research priority.

Key Words: self-harm, randomized controlled trials, meta-analysis

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Suicide is a global health problem and a major public health concern.[1,2] It is the second or the third leading cause of death in adolescents in the West and an important cause of death in developing countries.[2] In the United States, the research literature tends to distinguish between suicide attempts (defined as self-harm with some non-zero intent to die), non-suicidal self-injury (NSSI), and self-harm with undetermined intent.[3] In contrast, researchers in the United Kingdom and Europe frequently use the broader term "self-harm" to refer to self-poisoning or self-injury, irrespective of the intent.[4] Both suicide attempts and the broader self-harm category have been shown to be among the strongest predictors of death by suicide in adolescence, increasing the risk approximately 10-fold.[5,6]

The critical need for clinical guidance regarding optimal clinical intervention strategies for youths engaging in self-harm is underscored by research indicating the following: prior suicide attempts and self-harm broadly are strong predictors of suicide deaths[5,7]; among depressed adolescents and those at risk for depression, NSSI is a strong predictor of future suicide attempts[8-10]; and a substantial subgroup of youths who attempt suicide also engage in NSSI.[9] Self-harm, defined broadly, is also a common phenomenon: a systematic review of 128 studies reported a pooled lifetime prevalence of 13.2% (95% CI = 8.1–18.3).[11] Rates for self-harm (which include suicide attempts and NSSI) are higher than those for suicide attempts, currently estimated at an annual rate of 7.8%.[12]

This review and meta-analysis seek to extend and update a number of previous notable reviews of suicidal behavior and self-harm in adolescents that did not include meta-analyses[6,13] and were specifically focused on suicidal behavior[7,14,15]; non-suicidal self-harm only[16,17]; social factors linked with self-harm[18]; emergency management of self-harm[19] studies with mixed adult and adolescent samples[20]; or the etiological factors of self-harm.[21]

To our knowledge, this is the first published meta-analysis of randomized controlled trials (RCTs) evaluating therapeutic interventions (TIs) in reducing both suicidal behavior and nonsuicidal self-harm in adolescents.

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Supplemental material cited in this article is available online.

Consistent with recommendations from prior reviews, we examine effects for suicide attempts, NSSI, and undetermined self-harm separately, as well as report effects for self-harm as a broad category and explore potential moderators of treatment effects, including treatment dose and family involvement in treatment.

METHOD

For clarity, we state whether the results of the studies reviewed in this article apply to adolescents with self-harm, suicide attempts, or NSSI where these distinctions are clear. When we refer to "self-harm," we are referring to the broad definition used in the United Kingdom and Europe that includes NSSI, suicide attempts, and self-harm with undetermined intent. Self-harm is the primary outcome measure in this meta-analysis.

Inclusion Criteria

Inclusion criteria for the meta-analysis stipulated RCTs of specific TIs, defined as a theoretically coherent, manualized (or otherwise replicable) psychological, social, or pharmacological intervention, versus control treatment or placebo, in adolescents through age 18 years who have self-harmed at least once. A wide range of interventions was considered, independent of the theoretical underpinnings, including interventions focusing on young people, family-centered interventions, and interventions targeting wider social networks of the young people.

Exclusion Criteria

Exclusion criteria eliminated studies in which participants with self-harm were a minority of the study population (<50%); studies with self-harm occurring exclusively in the context of neurodevelopmental disorders (e.g., autism); or studies that did not conform to current criteria for evaluating methodological features of RCTs (Jadad score <2, an indicator of methodological quality/rigor, including blinding, allocation concealment, and accountability of all patients including withdrawals).[22]

Identification and Selection of Studies

We searched The Cochrane Central Register of Controlled Trials (4th edition, 2010), OVID Medline (Subject headings "Self-injurious Behavior," "Suicide, Attempted," "Self-Mutilation," "Suicide," "Overdose"), and then searched PsychINFO, EMBASE, and PubMed databases using equivalent subject headings. All databases were searched to May 2014.

Reference lists of the retrieved articles were examined for additional relevant publications, and cited articles were also searched. In addition, we searched clinical trials databases and contacted key investigators in the United Kingdom, United States, Norway, the Netherlands (Holland), and Australia, to obtain the results of any unpublished studies and to clarify details of the published ones.

No limits were applied to the search apart from study type (treatment studies, RCTs) and the age of participants (children and adolescents 0–18 years old).

The retrieved articles from each database were downloaded into EndNote (version X5), and all duplicates were removed.

The methodological quality of the studies was assessed using allocation concealment as a proxy.[23,24] Allocation concealment is a procedure for protecting the randomization process so that the treatment to be allocated is not known before the patient is entered into the study. We used the following quality ratings: 1 = adequate concealment (e.g., using opaque sealed envelopes); 2 = unclear concealment; and 3 = inadequate concealment (e.g., using open random number tables). We also calculated the Jadad score for each of the included studies.[22] In calculating the Jadad score, each study is evaluated according to the quality of randomization, blinding procedures, and description of withdrawals and dropouts. Jadad scores range from 0 to 5, with trials scoring 3 or greater considered good quality trials.

One of the authors (D.O.) screened the titles, abstracts, and full texts to assess the eligibility of the studies. The results were confirmed by an independent search performed by the second author (T.T.). Disagreements were resolved by consensus. A standardized data extraction sheet was used to collect data from eligible studies on the bibliographic details, self-harm definition, type of intervention, setting, and sociodemographic characteristics of the young persons and their families. The data were entered into a dedicated electronic database and checked for inconsistencies.

Statistical Analysis

In the calculation of pooled risk differences, we used the outcome of the proportion of the young persons who self-harmed at least once during the follow-up period of each study. We dichotomized young persons in each eligible study into 2 groups: those who self-harmed at least once, and those who never self-harmed for the duration of the longest follow-up period available. To calculate the pooled mean effect size, we used RevMan (Version 5.2), a computer program developed to support Cochrane reviews and meta-analyses. Each study was weighted in proportion to its sample size and tau^2 (the estimated variance of the true effect sizes). Sensitivity and meta-regression analyses were done using STATA 13.[25]

We calculated the I^2-statistic to estimate heterogeneity.[26] I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than sampling error and ranges between 0% (no inconsistency) and 100% (high heterogeneity) with values of 25%, 50%, and 75% suggesting low, moderate, and high heterogeneity. As there was evidence of significant heterogeneity between studies, we calculated pooled risk difference with random effect model only.[27] A random effect analysis model makes the assumption that individual studies are estimating different treatment effects due to the diversity of clinical interventions and methodological factors. We then repeated the meta-analysis for those studies targeting self-harm excluding suicide attempts and for the studies targeting suicide attempts alone. Sensitivity analyses were conducted to weigh up the relative influence of each individual study on the pooled effect size using STATA's user-written function "metainf."[28]

Finally, meta-regression was performed to assess the influence of the number of sessions (single/multiple), lengths of follow-up periods (months), family involvement (more than 50% of the total number of sessions/fewer than 50%), proportion of females, proportion of patients taking psychotropic medication, mean age (years), characterization of the control group (yes/no), quality of the study (high/low), and outcome measure (suicide only/suicide and self-harm) on the effect size using the user-written STATA function "metareg."[29]

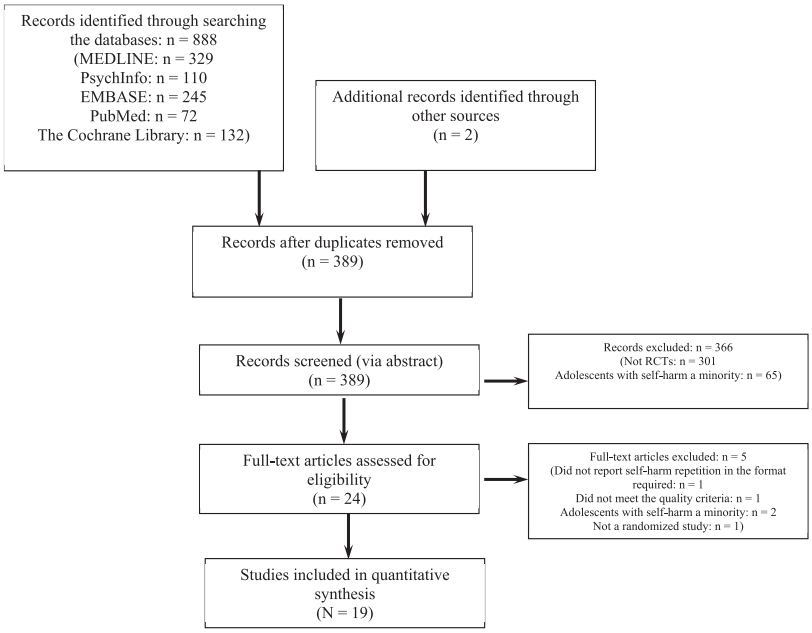
The presence of publication bias for the main experimental hypothesis of therapeutic intervention effects on suicide attempts and self-harm was assessed informally by a funnel plot and formally by its direct statistical analogues Begg's adjusted rank correlation test[30] and Egger's test,[31] which are implemented in STATA "metabias."

RESULTS

Included Studies

The original search resulted in the retrieval of 389 articles (Figure 1), and 23 of these were RCTs of TIs in children and

FIGURE 1 Flow of studies. Note: RCTs = randomized controlled trials.



adolescents with the presenting problem of self-harm; there were also 5 further RCTs in progress.[32-36] Nineteen of the studies met the inclusion criteria, including 1 study accepted for publication in July 2014.[37] Selected characteristics of these studies are presented in Table 1.[37-55] Of the 24 RCTs identified, 5 were eliminated: 2 RCTs[56,57] were excluded, as adolescents with self-harm likely comprised a minority of the study sample; 1 RCT[58] did not meet the minimum quality criteria; and 1 RCT[59] did not report self-harm in the format required. In addition, 1 study was not included, as the majority of the young persons in the study were not randomized.[60] The quality of the studies was variable; random allocation concealment was evident in 11 of the 19 studies, and it was unclear in the rest. The Jadad score was 3 for 11 studies and it was 2 for 8 studies. There were no disagreements between the 2 raters regarding the quality of the studies.

The trials included in this meta-analysis reported the effects of a wide variety of TIs covering both individual and group treatments (Table 2[38-50]): specific problem-solving intervention designed to increase engagement[41]; cognitive-behavioral treatment targeting problem solving and affect management skills[43]; home-based family therapy delivered by social workers[39]; developmental group psychotherapy incorporating the techniques of problem solving and cognitive-behavioral interventions, dialectical behavior therapy, and psychodynamic group psychotherapy[40,46,50]; individual cognitive analytic therapy designed to prevent the development of borderline personality disorder[45]; attachment-based family therapy[49]; therapeutic assessment for self-harm[55,61]; emotion regulation group training[47,54]; issuing tokens allowing readmission[38]; youth-nominated support team[44,48]; the Family Intervention for Suicide Prevention[51]; cognitive-behavioral therapy[52]; mentalization-based therapy[53]; multisystemic therapy[42]; and dialectical behavior therapy.[37] These interventions were compared to a range of control treatments, including most commonly treatment as usual (TAU), but also enhanced TAU; assessment as usual (2 studies); supportive relationship treatment (1 study); and hospitalization (1 study). For convenience we will refer to these control treatments as "treatment as usual" (TAU).

Effects of TIs Versus TAU on Self-Harm

First, we examined the overall effect of TIs versus TAU for any self-harm, including suicide attempts, NSSI, and/or self-harm with ambiguous intent. Results are shown in Figure 2; the pooled risk difference for any self-harm of TIs was −0.07 (95% CI = −0.01 to −0.13), z = 2.31, p = .02. The pooled difference between the risk of self-harm in the TIs arm (28.3%) and in the TAU arm (33.2%) produced an absolute risk reduction of 4.99%. Applying the 4.99% (95% CI = 1.01%–8.97%) absolute risk reduction found in the meta-analysis produced a number needed to treat (NNT) to prevent 1 episode of self-harm of 21 (95% CI = 11.2–98.5) over an average of 10 months (SD = 6.8 months). Using the pooled risk difference (0.07) changed this NNT to 14 (95% CI = 7.7–100). Using the pooled risk difference for suicide attempts produced an NNT of 33 (95% CI = cannot be estimated) and the NNT for nonsuicidal self-harm (including NSSI and self-harm with ambiguous intent) of 10 (95% CI = 4.8 to infinity).

The robustness of the estimate of pooled risk difference for any self-harm repetition was examined by sequentially removing each study and reanalyzing the remaining datasets. The estimated risk difference ranged from −0.085 (95% CI = −0.144 to −0.025)[46] to −0.041 (95% CI = −0.088 to 0.005).[37] Except for the analysis with 1 study removed

TABLE 1 Selected Characteristics of the Randomized Controlled Trials Reporting the Effects of Therapeutic Interventions (TIs) Versus Control Treatments on Self-Harm in Adolescents

Study, Country	Inclusion Criteria	Age (y)	Control	N	Interventions	ITT	Allocation	Self-Harm Ascertainment	Follow-Up (mo)
Cotgrove *et al.*, UK[38]	Hospital presentation with an episode of self-harm	<17 (mean 14.9)	Assessment as Usual	105	Assessment as usual and token allowing readmission	Participants randomized	Not specified	Clinical records	12
Harrington *et al.*, UK[39]	Self-poisoning cases referred to mental health teams	<16 (mean 14.5)	TAU	162	Home-based family intervention + TAU	Participants randomized	Concealed	Clinical interview	6
Wood *et al.*, UK[40]	Repeat self-harmers referred to an out-patient service	12–16	TAU	63	Developmental group psychotherapy + TAU	Participants randomized	Concealed	Clinical interview	7
Spirito *et al.*, US[41]	Suicide attempters receiving care in ED or pediatrics ward	12–18	Standard disposition planning	76	Compliance enhancement and standard disposition planning	Participants completing treatment	Not specified	Clinical interview	3
Huey *et al.*, US[42]	Psychiatrically hospitalized suicide attempters or patients with significant suicidality	10–17	Hospitalization	70	Multisystemic therapy	Participants completing treatment	Not specified	Caregiver report	12
Donaldson *et al.*, US[43]	Suicide attempters presenting to ED or inpatient unit	12–17	Supportive relationship treatment	39	Skills-based treatment	Participants starting treatment	Not specified	Clinical interview	6
King *et al.*, US[44]	Psychiatrically hospitalized suicide attempters or patients with significant suicidality	12–17	TAU	289	Youth-nominated support team-Version 1 + TAU	Participants randomized	Unclear using a random numbers table (even/odd assignment).	Clinical interview and self-report	6
Chanen *et al.*, Australia[45]	Outpatients with at least 2 *DSM-IV* criteria for borderline personality disorder + specified risk factors for BPD	15–18	Standardized good clinical care	86	Cognitive analytic therapy	Participants randomized	Concealed	Clinical interview	24
Hazell *et al.*, Australia[46]	At least 2 episodes of self-harm, one in past 3 mo, referred to outpatient service	12–16	TAU	72	Developmental group psychotherapy + TAU	Participants randomized	Concealed	Clinical interview	12
Schuppert *et al.*, Holland[47]	Outpatients with 2 or more symptoms of borderline personality disorder	14–19	TAU	43	Emotion regulation group training	Participants completing treatment	Not specified	Clinical interview and self-report	4 (end of treatment)
King *et al.*, US[48]	Psychiatrically hospitalized suicide attempters or patients with significant suicidality	13–17	TAU	448	Youth-nominated support team	Participants randomized	Concealed	Clinical interview and self-report	12
Diamond *et al.*, US[49]	Score >31 on the Suicidal Ideation Questionnaire (SIQJR) and score >20 on the Beck Depression Inventory (BDI-II), identified in primary care and emergency departments	12–17	Enhanced usual care	66	Attachment-based family therapy	Participants randomized	Concealed	Clinical interview	6

TABLE 1 Continued

Study, Country	Inclusion Criteria	Age (y)	Control	N	Interventions	ITT	Allocation	Self-Harm Ascertainment	Follow-Up (mo)
Green *et al.*, UK[50]	Outpatients with a history of at least 2 episodes of self-harm within the previous 12 mo	12–17	TAU	336	Developmental group psychotherapy + TAU	Participants randomized	Concealed	Clinical interview	12
Asarnow *et al.*, US[51]	ED presentation with suicide attempt or ideation	10–18	TAU	181	Family intervention for suicide prevention	Participants randomized	Concealed	Clinical interview and self-report	~2
Esposito-Smythers *et al.*, US[52]	Inpatients with a suicide attempt in the previous 3 mo or severe suicidal ideation and an alcohol or cannabis use disorder	13–17	Enhanced TAU	40	CBT for suicidality and substance misuse	Participants randomized	Not specified	Clinical interview	18
Rossouw and Fonagy, UK[53]	Outpatients with at least 1 episode of self-harm in the previous mo	12–17	TAU	80	MBT-A	Participants randomized	Concealed	Clinical interview and self-report	12
Schuppert *et al.*, Holland[54]	Outpatients with 2 or more symptoms of borderline personality disorder	14–19	TAU	109	Emotion Regulation Group Training	Participants completing treatment	Not specified	Clinical interview and self-report	4 (end of treatment)
Ougrin *et al.*, UK[55]	Urgent hospital/community presentation with an episode of self-harm	12–18	Assessment as usual	70	Assessment as Usual and Therapeutic Assessment	Participants randomized	Concealed	Clinical records	24
Mehlum *et al.*, Norway[37]	Outpatients with at least 2 episodes of self-harm, at least 1 within the last 16 wks	12–18	Enhanced usual care	77	DBT-A	Participants randomized	Concealed	Clinical interview	4

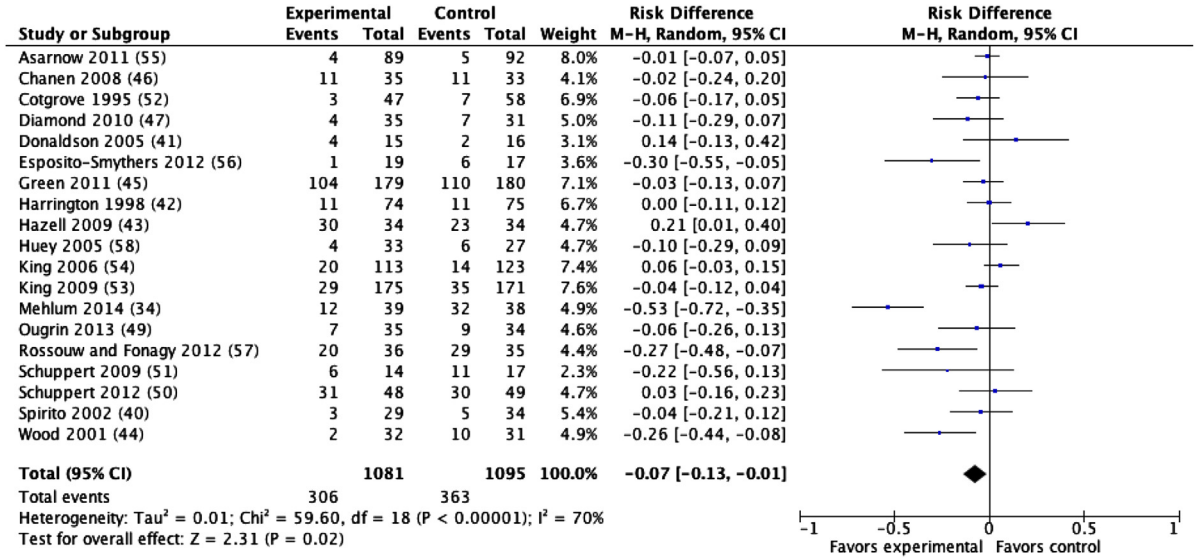
Note: CBT = cognitive-behavioral therapy; DBT-A = dialectical behavior therapy for adolescents; ED = emergency department; ITT = intention to treat; MBT-A = mentalization-based treatment for adolescents; RCT = randomized controlled trial; TAU = treatment as usual.

TABLE 2 Participants' Flow and Self-Harm in the Randomized Controlled Trials (RCTs) Reporting the Effects of Therapeutic Interventions (TIs) Versus Control Treatments in Adolescents

Study	Eligible	Randomized		Self-Harm Definition	Self-Harm Follow-Up Data Available	Participants With at Least 1 Episode of Self-Harm at Baseline		Participants Who Self-Harmed During the Follow-Up Period	
		TI	TAU			TI	TAU	TI	TAU
Cotgrove *et al.*, UK[38]	134	47	58	At least 1 suicidal or nonsuicidal self-harm episode	105	47	58	3/47	7/58
Harrington *et al.*, UK[39]	288	85	77	At least 1 suicidal or nonsuicidal self-harm episode	149	85	77	11/74	11/75
Wood *et al.*, UK[40]	83	32	31	Two or more suicidal or nonsuicidal self-harm episodes	63	32	31	2/32	10/31
Spirito *et al.*, US[41]	82	36	40	At least 1 suicide attempt	63	36	40	3/29	5/34
Huey *et al.*, US[42]	60	33	27	At least 1 suicide attempt	60	33	27	4/33	6/27
Donaldson *et al.*, US[43]	44	21	18	At least 1 suicide attempt	31	21	18	4/15	2/16
King *et al.*, US[44]	986	151	138	At least 1 suicide attempt	236	86	104	20/113	14/123
Chanen *et al.*, Australia[45]	106	44	42	At least 1 suicidal or nonsuicidal self-harm episode	68	31/41	25/37	11/35	11/33
Hazell *et al.*, Australia[46]	138	35	37	At least 1 suicidal or nonsuicidal self-harm episode	68	35	37	30/34	23/34
Schuppert *et al.*, Holland[47]	Not reported	23	20	At least 1 suicidal or nonsuicidal self-harm episode	31	15	15	6/14	11/17
King *et al.*, US[48]	1,050	223	225	At least 1 suicide attempt	346	169	162	29/175	35/171
Diamond *et al.*, US[49]	85	35	31	At least 1 suicide attempt	66	19	22	4/35	7/31
Green *et al.*, UK[50] Asarnow et al., US[51]	394	183	183	At least 1 suicidal or nonsuicidal self-harm episode	359	183	183	145/181[a] 104/179[b]	142/181[a] 110/180[b]
Esposito-Smythers *et al.*, US[52]	181	89	92	At least 1 suicide attempt	139	63	77	4/62	5/77
Rossouw and Fonagy, UK[53]	64	20	20	At least 1 suicide attempt	32	15	15	1/19	6/17
Diamond *et al.*, US[49]	133	54	55	At least one suicidal or nonsuicidal self-harm episode	97	36	39	31/48	30/49
Green *et al.*, UK[50]	110	40	40	At least 1 suicidal or nonsuicidal self-harm episode	71	40	40	20/36	29/35
Ougrin *et al.*, UK[4]	78	35	35	At least 1 suicidal or nonsuicidal self-harm episode	69	35	35	7/35	9/34
Mehlum *et al.*, Norway[37]	165	39	38	At least 1 suicidal or nonsuicidal self-harm episode	77	39	38	12/38	32/39

Note: TAU = treatment as usual.
[a]*0- to 6-month follow-up.*
[b]*6- to 12-month follow-up.*

FIGURE 2 Effects of therapeutic interventions (TIs) versus treatment as usual (TAU) on self-harm in adolescents. Note: M-H = Mantel-Haenszel.



($p = .08$),[37] all effect sizes remained significantly different from 0. The significant overall effect size was unlikely to be determined by a single study given the small total number of studies and the lower power after sequentially removing each study.

Next we conducted separate analyses examining effects of TIs on suicide attempts and on other forms of self-harm (NSSI and self-harm behavior with ambiguous intent). Results indicated a nonsignificant effect for TIs versus TAU on suicide attempts (risk difference: −0.03, 95% CI = −0.09 to 0.03, z = 0.93, $p = 0.35$) (Figure 3). Results focusing on nonsuicidal self-harm (excluding suicide attempts) showed a reduction in the pooled risk of self-harm compared to TAU, although this was not statistically significant at the 5% level (risk difference = −0.1, 95% CI = −0.21 to 0.00, z = 1.91, $p = .06$; see Figure S1, available online).

As a sensitivity analysis, we performed the meta-analysis with the eight studies with the Jadad score of 2 excluded. The summary effect remained robust with the remaining 11 TIs versus TAU showing a reduction in the likelihood of self-harm (risk difference = −0.09, 95% CI = −0.18 to −0.01, z = 2.10, $p = .04$; see Figure S2, available online).

Meta-Regression

Nine meta-regressions were performed to assess the influence of the number of sessions (single versus multiple); lengths of follow-up periods (months); presence or absence of significant family treatment component in the experimental treatment; proportion of females; proportion of patients taking psychotropic medication; mean age (years); characterization of the control group (manualized or unspecified); quality of the study (Jadad score of 2 versus 3); and outcome measure (suicide attempts or any nonsuicidal self-harm) on the effect size. None of the study characteristic variables showed a significant moderating effect on outcome. The mean difference of risk reduction between trials with multiple and single sessions was −0.045 (−0.24 to 0.14, t = −0.5, $p = .62$; n = 19 [a negative sign means that the first level here, "multiple sessions," resulted in a stronger risk reduction than the second level, "single session"]); length of follow-up periods (months): 0.0005 (95% CI = −0.0128 to 0.0138), t = 0.006, $p = .94$, n = 19; presence and absence of family component: −0.111 (95% CI = −0.265 to 0.043), t = −1.52, $p = .15$, n = 19; percentage of females: 0.00034 (95% CI = −0.0064 to 0.00704), t = 0.11, $p = .915$, n = 19; percentage of patients taking psychotropic medication: 0.0042 (95% CI = −0.003 to 0.0115), t = 1.34, $p = .22$, n = 10; mean age (years): −0.0334 (95% CI = −0.1607 to 0.0939), t = −0.56, $p = .59$, n = 18; characterized and uncharacterized control group: −0.122 (95% CI = 0.337–0.100), t =−1.22, $p = .24$, n = 15; high and low quality of study: −0.048 (95% CI = −0.214 to 0.118), t = −0.61, $p = .55$, n = 19; and suicide attempts and nonsuicidal self-harm: 0.058 (95% CI = −0.104 to 0.21), t = 0.75, $p = .46$, n = 19 were all nonsignificant. Studies with strong family component (risk reduction −0.14 [95% CI = −0.27 to −0.02]) and studies with multiple treatment sessions (risk reduction −0.09 [95% CI = −0.017 to 0.00]) were associated with significant reduction of self-harm, unlike studies with weak family involvement and studies of TIs with single sessions.

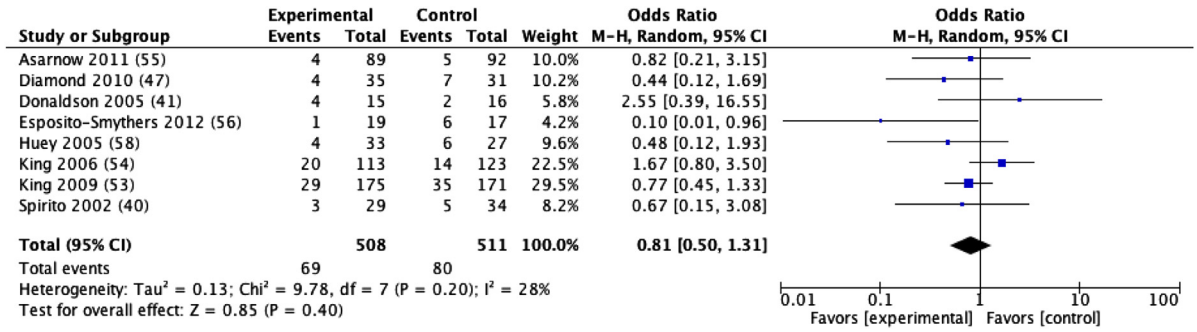
Funnel Plots and Risk of Bias

The funnel plots of the 3 meta-analyses are shown in Figure S3 (available online). There was little evidence of funnel plot asymmetry in the meta-analysis, which suggests that there is no serious publication bias. Results of both Begg's and Egger's tests for publication bias were nonsignificant ($p = .16$ and $p = .11$, respectively).

DISCUSSION

The results of the present study support the value of TIs in the reduction of self-harm as a global category (including any self-harm), and show that when the effects of TIs are

FIGURE 3 Effects of therapeutic interventions (TIs) versus treatment as usual (TAU) on suicide attempts in adolescents. Note: M-H = Mantel-Haenszel.



examined separately for suicide attempts and NSSI, effects are weaker, with the strongest effect for NSSI and a weaker effect for suicide attempts. Although the results on self-harm as a global category are encouraging, particularly given data from 3 major studies indicating that NSSI is a strong predictor of future suicide attempts,[8-10] our results on suicide attempts underscore the gaps in knowledge regarding optimal treatment strategies for reducing the risk of suicide attempts. The NNT (14 to prevent 1 incident of self-harm) also underscores the importance of continued research in this area. This NNT, however, compares favorably to many other medical interventions such as statins for cardiovascular events in high-risk groups (>20),[62] extended release valproate for bipolar disorder in adolescents (100),[63] or phototherapy for jaundiced babies (222–333).[64]

The effects of TIs for self-harm as a global category versus TIs for suicide attempts specifically are of interest. Subgroup analyses indicated that the pooled effect of the studies investigating TIs for self-harm excluding the studies purely focused on suicide attempts remained similar to the overall conclusions of the meta-analysis (although just escaping the arbitrary statistical significance threshold, $p = .06$ versus $p < .05$). However, this was not true for the studies purely focused on suicide attempts.

One possible explanation is that our subgroup analysis lacked power to demonstrate efficacy of TIs for suicide attempts. This is partly due to the lower frequency of suicide attempts relative to NSSI, which makes it harder to detect effects of TIs on suicide attempts. This may also point to some important differences between suicidal and nonsuicidal self-harm that may go beyond phenomenology and extend to the differences in treatment response.[65] It may also indicate that strategies aiming to reduce NSSI should differ from those aiming to reduce recurrent suicide attempts.

In considering the results of this meta-analysis, several limitations merit note. First, insufficient good-quality, independently replicated RCTs have been conducted to draw firm conclusions about the effectiveness of specific TIs for self-harm in adolescents. Indeed, the only treatment subjected to independent replication (developmental group therapy) was not associated with reduced self-harm in 2 replication trials. At present there are no published RCTs of pharmacological agents specifically targeting self-harm in adolescents, or RCTs evaluating combined pharmacological and psychosocial treatments. In addition, there are open trials with promising treatments targeting suicide attempt reduction that have not yet been tested in RCTs, and there are RCTs in progress.[32-36] Finally, 2 of the trials included in our meta-analysis were powered to detect changes in treatment adherence and focused on improving linkage to outpatient treatment after emergency treatment for suicidal behavior and self-harm.[51,62] Given the known problems with treatment adherence in this group of young persons, improving treatment adherence is viewed as a critical first step for delivering effective treatment and reducing suicide/self-harm risk. As indicated by our findings on treatment dose, these studies had weak effects on self-harm outcomes and weakened overall effect sizes in the meta-analysis. More work is required to translate this improved engagement into clinically meaningful outcomes, given the absence of significant effects of these treatment-engagement–focused interventions on self-harm and results suggesting minimal benefits of linkage to community TAU.[51]

We considered methodological rigor in the meta-analysis, and sensitivity analyses excluding studies with lower rigor (defined as Jadad scores ≤ 2) confirmed the primary analyses. However, many of the studies included in this review are limited by small sample sizes, poorly characterized and nonmanualized TAU conditions (with some exceptions),[43,45] and exclusion before randomization or loss to follow-up of a substantial number of potential participants. There was significant diversity of clinical interventions and methodological differences, which forced us to use a random effects model. This model does not assume a single treatment effect but rather a distribution of treatment effects, and therefore the estimated effect size needs to be interpreted as the average treatment effect. Furthermore, exploratory analyses examining the impact of specific treatment components had limited statistical power. The effect sizes of the TIs with strong family components and substantial treatment dose underscore the potential importance of these intervention components. As most of the included studies had relatively brief durations of postintervention follow-up, longer-term intervention effects remain to be determined.

In the leave-one-out analysis, the pooled risk difference for any self-harm repetition was not significant when the Mehlum *et al.*[37] study was omitted. This study differed significantly from the other studies in several ways. The

therapists delivering DBT underwent lengthy training with ongoing supervision. The focus of the intervention was on developing skills of both young persons and their parents. The format of the intervention included a prominent group component. The duration of the intervention was relatively long at 19 weeks on average. These features may be important in designing clinical interventions for young persons with self-harming tendencies.

Further limitations of this meta-analysis include the relatively small number of extant studies and cross-study variation in definitions of self-harm. Finally, although the pooled efficacy of TIs versus TAU for self-harm in this meta-analysis is statistically significant, the clinical interpretation is difficult because of a very large heterogeneity. This heterogeneity in conjunction with the absence of successful replications underscores the crucial need for additional research to advise service providers, service commissioners, and funding agencies about the optimal forms of TIs to invest in. Linked to this, little knowledge exists about the mechanism of action for TIs in the treatment of adolescent self-harm; this is an important future avenue of research.

There have been many previous reviews in this area with often-conflicting conclusions. In contrast to some reviews,[19,20] partly due to the more stringent criteria used in this meta-analysis, we did not find sufficient evidence to recommend any specific intervention to reduce self-harm. Inspection of effects of individual studies suggests that DBT, other CBTs, and MBT may be good candidates for this, particularly as suggested in other reviews when delivered with a family component and a substantial number of treatment sessions.[16,17] Above all and in line with other reviews' recommendations, more research and replication of the positive findings by independent groups are urgently required.

Therapeutic interventions to prevent self-harm appear to be effective. Additional research and replication studies are critically needed to identify specific interventions with replicated efficacy and effectiveness in routine clinical settings, the mechanisms through which interventions reduce self-harm risk, and those variables most important for matching specific youths and families to the interventions with greatest likelihood of benefits.

More research is urgently needed to establish effective treatment for self-harming adolescents. Greater international consensus regarding definitions and measurement strategies for self-harm behaviors will strengthen efforts to advance research and practice. &

CG Clinical Guidance

- A wide variety of therapeutic interventions (TI) are now available for the treatment of self-harm in adolescents.
- TIs appear to reduce self-harming behavior.
- TIs with the largest effect sizes are dialectical behavior therapy (DBT), cognitive-behavioral therapy (CBT), and mentalization-based therapy (MBT).
- No TI has had its efficacy independently replicated.
- Little knowledge exists about the precise mechanism of action for TIs in the treatment of adolescent self-harm.
- Independent replication of the results achieved by DBT, MBT, and CBT is now urgently required.

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Correspondence to Dennis Ougrin, MBBS, MRCPsych, PGDip(Oxon), PhD, King's College London, Child and Adolescent Psychiatry, Institute of Psychiatry, PO85, De Crespigny Park, London SE5 8AF, UK; e-mail: dennis.ougrin@kcl.ac.uk

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FIGURE S1 Effects of therapeutic interventions (TIs) versus treatment as usual (TAU) on nonsuicidal self-harm in adolescents. Note: M-H = Mantel-Haenszel.

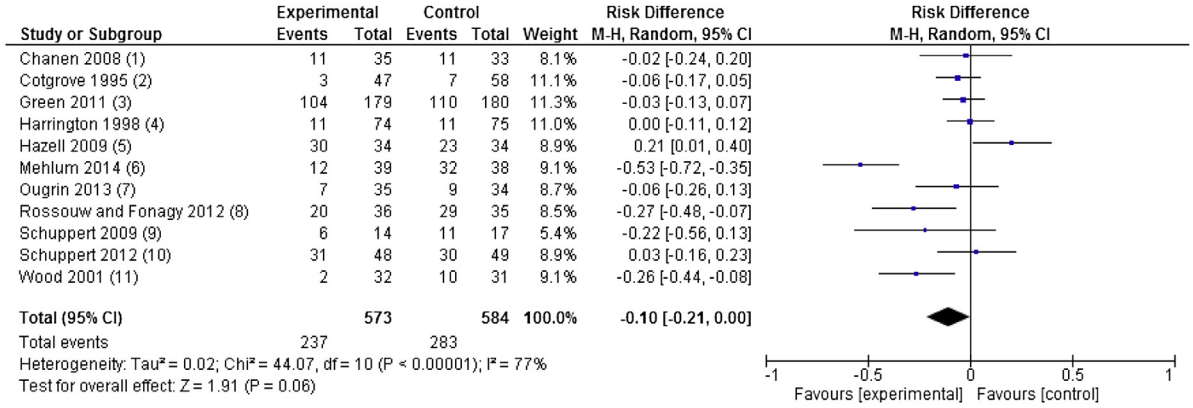

FIGURE S2 Therapeutic interventions (TIs) versus treatment as usual (TAU) for self-harm in adolescents studies with Jadad score >2. Note: M-H = Mantel-Haenszel.

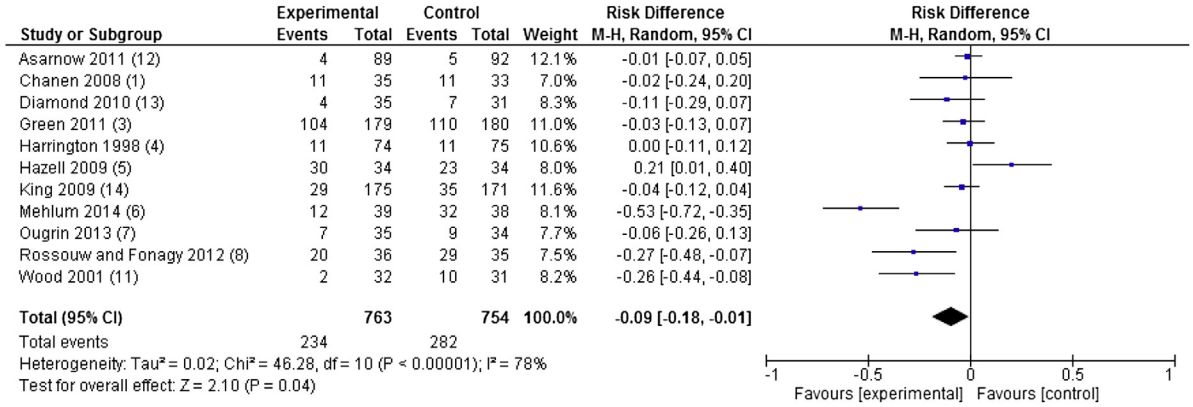

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FIGURE S3 Funnel plots of the studies of therapeutic interventions (TIs) versus treatment as usual (TAU) for suicide attempts (a), self-harm without suicide attempts (b), and all self-harm (c). Note: OR = odds ratio; RD = risk difference; SE = standard error.