META-ANALYSIS

Systematic Review and Individual Participant Data Meta-Analysis: Reducing Self-Harm in Adolescents: Pooled Treatment Effects, Study, Treatment, and Participant Moderators

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Objective: Self-harm is common in adolescents and a major public health concern. Evidence for effective interventions that stop repetition is lacking. This individual participant data (IPD) meta-analysis of randomized controlled trials (RCTs) aimed to provide robust estimates of therapeutic intervention effects and explore which treatments are best suited to different subgroups.

Method: Databases and trial registers to January 2022 were searched. RCTs compared therapeutic intervention to control, targeted adolescents ages 11 to 18 with a history of self-harm and receiving clinical care, and reported on outcomes related to self-harm or suicide attempt. Primary outcome was repetition of self-harm 12 months after randomization. Two-stage random-effects IPD meta-analyses were conducted overall and by intervention. Secondary analyses incorporated aggregate data from RCTs without IPD.

Results: The search identified 39 eligible studies; 26 provided IPD (3,448 participants), and 7 provided aggregate data (698 participants). There was no evidence that interventions were more or less effective than controls at preventing repeat self-harm by 12 months in IPD (odds ratio 1.06 [95% CI 0.86, 1.31], 20 studies, 2,949 participants) or IPD and aggregate data (odds ratio 1.02 [95% CI 0.82, 1.27], 22 studies, 3,117 participants) meta-analyses and no evidence of heterogeneity of treatment effects on study and treatment factors. Across all interventions, participants with multiple prior self-harm episodes showed evidence of improved treatment effect on self-harm repetition 6 to 12 months after randomization (odds ratio 0.33 [95% CI 0.12, 0.94], 9 studies, 1,771 participants).

Conclusion: This large-scale meta-analysis of RCTs provided no evidence that therapeutic intervention was more, or less, effective than control for reducing repeat self-harm. Evidence indicating more effective interventions in youth with 2 or more self-harm incidents was observed. Funders and researchers need to agree on a core set of outcome measures to include in subsequent studies.

Plain language summary: Self-harm is common in adolescents and linked to higher risks of repeated self-harm and suicide. This meta-analysis of 33 randomized controlled trials involving 4,146 adolescents found that therapeutic interventions were no more effective than standard care at preventing repeat self-harm at 12 months. However, interventions were more effective in youth with 2 or more self-harm incidents. The authors discuss limitations posed by the lack of uniform outcome measures for self-harm.

Clinical guidance

- No single, specific intervention can be conclusively recommended for preventing repetition of self-harm in youth.
- Young people with multiple prior episodes of self-harm are at heightened risk and may be more likely to benefit from treatment.

Study preregistration information: Reducing Self-harm in Adolescents: An Individual Participant Data Meta-analysis; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=152119.

Key words: adolescents; IPD meta-analysis; self-harm; suicide; systematic review

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Self-harm in adolescents is a major public health concern in the United Kingdom and globally,[1] with lifetime prevalence of 16.9% and increasing rates.[2] Following self-harm, suicide attempt is common[3] and is the second commonest cause of death in children and adolescents 10 to 24 years old.[4] All-cause mortality shows a 4-fold increase and death by suicide shows a 10-fold increase[5] following self-harm. Nonfatal repetition of self-harm is common with a 1-year hospital reattendance rate of 18%.[6]

Interpretation of the literature is complicated by the lack of clarity regarding definitions of self-harm. Harris *et al.*[7] conducted a meta-analysis of self-injurious thoughts and behaviors in which definitions of self-harm were based on the presence or absence of suicidal intent. Intentional self-directed harm without suicidal intent was considered as nonsuicidal self-injury (NSSI); suicide-related cognitions and plans, as suicidal ideation; self-directed harm with intent to die, as a suicide attempt; and when no information regarding suicidal intent is provided, as self-harm. However, determining suicidal intent is not straightforward. Classifying self-harm by suicidal intent and method, for example, NSSI or not, may be clinically misleading given that so many patients presenting to hospital switch method.[8]

In this study, we use the generic term self-harm defined by the UK National Institute for Health Care Excellence (NICE) as any form of nonfatal self-poisoning or self-injury (including cutting, taking excess medication, attempted hanging, self-strangulation, jumping from height, running into traffic), regardless of suicidal intent.[9] It thus includes NSSI as defined by Harris *et al.*,[7] but excludes suicidal ideation.

Effective interventions to prevent repeat self-harm have not yet been identified despite several published studies, systematic reviews, and aggregate data meta-analyses. The most recent Cochrane review, published in 2021,[10] used tight eligibility criteria and included only randomized controlled trials (RCTs) with comparisons of specific interventions in children and adolescents with a recent (within 6 months of trial entry) episode of self-harm resulting in presentation to the hospital or clinical services. The authors identified only 17 studies (2,280 participants) and found "only uncertain evidence regarding a number of psychosocial interventions in children and adolescents who engage in SH [self-harm]"[10(p2)] and suggested that further evaluation of dialectical behavior therapy for adolescents (DBT-A) was warranted. Kothgassner *et al.*[11] used similar eligibility criteria in their review, but past self-harm was necessary only at some point in the past, not within 6 months as with the Cochrane review. They identified 25 studies with 2,962 participants. In both reviews,[10,11] about one-third of participants were from 1 study.[12] Kothgassner *et al.*[11] concluded that participants receiving therapeutic interventions fared slightly better than active controls but could not identify a single specific intervention, although there were small positive effects for DBT-A and family-centered therapy. Using similar eligibility criteria, the most recent UK NICE guideline[9] also recommended consideration of DBT-A for children and young people.

Harris *et al.*[7] took a different approach with much wider definitions of self-harm. They included studies that explored only impact on suicidal ideation, as well as studies where the primary target of intervention was a mental disorder such as depression, but where self-harm had been measured as an outcome. However, this approach produced similar findings: "Nearly all interventions produced nonsignificant reductions in SITBs [self-injurious thoughts and behaviors]."[7(p1)]

In adults, the picture is similar. Whilst the most recent Cochrane review found promising findings for CBT-based and dialectical behaviour therapy, it emphasised the need for further investigation and "There were only a few, generally small trials on most other types of psychosocial therapies, providing little evidence of beneficial effects".[13] Fox et al. found only small intervention effects—"no intervention appeared significantly and consistently stronger than others."[14(p1)]

Reviews in both adults and children highlight the relatively low number of high-quality RCTs alongside the generally poor quality of many of the studies reviewed despite the significant scale of the problem and the lack of recognized effective interventions. One plausible hypothesis for the lack of effective interventions is that samples aggregate young people who have engaged in self-harm for different reasons and apply a one-size-fits-all intervention. Identification of relevant subgroups within young people who engage in self-harm may offer a more promising path forward.

An individual participant data (IPD) meta-analysis, by reanalyzing pooled data from eligible studies, can provide more robust estimates of the effects of therapeutic interventions for self-harm than conventional meta-analyses that rely on aggregate data (AD) and reported analyses.[15] IPD allow for the inclusion of subsets of participants, thereby increasing the number of studies and participants

contributing to analyses, which enhances the power to detect effects. In many of the aforementioned reviews, good-quality RCTs had to be excluded because authors could not disaggregate data when not all participants met the review inclusion criteria, for example, such as by age or type of self-harm. Factors at the participant, treatment, and study levels all may influence the effectiveness and outcomes of interventions.[10,11,16] IPD enable analyses of the potential moderating effects of participant-level factors on outcomes, which is often limited in AD meta-analyses.

We hypothesized that an IPD meta-analysis would allow us to retain the stringent eligibility criteria of reviews such as Cochrane, while including significantly more studies and participants. In cases where authors of eligible studies were unable to share data, we could still incorporate published AD on eligible participants, as in standard meta-analysis, alongside our IPD analyses. This approach not only would provide more accurate information about the effectiveness of interventions to prevent self-harm, but also would allow us to explore study and treatment moderators. Additionally, it would enable us to investigate participant-level moderators of treatment effects, potentially identifying subgroups of adolescents who might benefit from specific therapeutic interventions for self-harm. The protocol[17] and a description of the search methods, how we accessed IPD, risk of bias assessment, and outputs are published elsewhere.[18]

METHOD

This study, Reducing Self-harm in Adolescents: An Individual Participant Data Meta-analysis (RISA-IDA), is registered on PROSPERO,[19] and the report follows PRISMA-IPD reporting guidelines (Supplement 1, available online).[20] The study was conducted following a successful bid for a commissioned call from the National Institute for Health and Care Research (NIHR), which specified the need to conduct an IPD meta-analysis.

Eligibility Criteria and Search Strategy

Self-harm was defined as any form of nonfatal self-poisoning or self-injury (including cutting, taking excess medication, attempted hanging, self-strangulation, jumping from height, running into traffic), regardless of suicidal intent.[9] This includes definitions of NSSI commonly used by US researchers and suicidal behavior, where lack of intent is assumed by reference to the method of self-harm. Self-harm could be self-reported, reported via interview, or identified through hospital or medical records.

The inclusion criteria were as follows:

1. RCTs comparing any intervention delivered in outpatient/community settings aiming to reduce subsequent self-harm against any control (studies where the intervention primarily targeted underlying pathology, for example, depression, and self-harm was measured only as a secondary outcome were excluded)
2. Adolescents ages 11 to 18 who had engaged in self-harm at least once before randomization and presented to clinical services for self-harm (includes suicide attempt but excludes suicidal ideation without explicit self-harm)
3. Data collected relating to self-harm or suicide attempt

We incorporated studies in which only a subset of participants met our criteria if IPD could be obtained for them: ages 11 to 18 and having engaged in self-harm at least once before randomization. We excluded studies of intensive inpatient and prevention-based interventions not targeted specifically at adolescents who presented to clinical services with self-harm and studies with less than 20 eligible participants.

We identified eligible studies (Supplement 2, available online) via a search for systematic reviews of self-harm in adolescents conducted in June 2019 and searches for recent publications from 2015 (the date of the last comprehensive search reported in the most recent systematic review) to August 2019, updated in February 2021 and January 2022. This search included unpublished trials (no date restriction) and ongoing RCTs.

Our literature search is described in full elsewhere.[18] Two authors (A.W.-H., D.C.) independently reviewed titles, abstracts, and full texts in Covidence. Disagreements were resolved by discussion and where necessary adjudicated by a third author (R.W.).

Interventions

Therapeutic interventions were grouped by consensus (D.C., D.O., P.F.), according to study published descriptions, theoretical underpinnings, supplementary material, and manuals. The categories were cognitive-behavioral therapy (CBT); DBT; family therapy; group therapy; cognitive analytic therapy and mentalization-based therapy (CAT/MBT); multisystemic therapy; problem solving, psychoeducation, support (PST); postcards, tokens, documents (postcards/tokens); and other single-session, brief interventions. Control treatments were treatment as usual (TAU), enhanced TAU, or active control.

Outcome Measures

The primary outcome was repetition of self-harm, from randomization to the last available follow-up within 3, 6, 12, 18, and 24 months after randomization. The primary

time period was 12 months, including studies where the follow-up assessment of self-harm was >6 and ≤12 months.

Secondary outcomes were time to repetition of self-harm; pattern of self-harm repetition between 6 and 12 months, 12 and 18 months, and 18 and 24 months after randomization; general psychopathology (aggregated symptom scores of any mental disorder); depression; and suicidal ideation. Additional outcomes (descriptive analysis only) were quality of life and death of adolescent. Follow-up was grouped as follows: <=3-months, 6 (>3 to <=6), 12 [>6 to ≤12], 18 [>12 to ≤18], 24 [>18 to ≤24], and ≥24 months after randomization.

Data Collection

We sought IPD, including baseline participant demographics and clinical data, details of therapeutic intervention, and outcomes, prioritizing the primary outcome. More detail about how IPD were accessed is available elsewhere.[18] Where IPD were not available, AD were extracted from study reports and publications, where possible, by A.W.-H. (verified by D.S.). Study-level variables relating to study conduct and design, methodology, and clinical factors were extracted from publications by A.W.-H. (verified and categorized by D.C.).

Risk of Bias in Individual Studies

Pairs of authors (D.C., F.M., A.T., E.D.) independently assessed the quality of included studies using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB2),[21] providing up to 2 RoB2 assessments for each study for each method of data collection. Disagreements were resolved through discussion and consultation with a third reviewer (A.W.-H.).

Statistical Analysis

Data were analyzed using SAS 9.4[22] and STATA 17.[23] Analyses were based on intention to treat, including all participants as randomized, regardless of withdrawal or protocol compliance. Primary analyses were based on available data, conducted separately for each time period, overall and by therapeutic intervention.

Treatment effects are expressed as odds ratios (ORs), hazard ratios, and SMDs. ORs of <0.59 or >1.68, <0.29 or >3.47, and <0.15 or>6.71[24] and absolute SMDs of 0.2, 0.5, and 0.8 are used to describe small, moderate, and large (positive or negative) effects.[25] For repetition of self-harm outcomes, ORs <1 represent reduced odds of self-harm in the intervention compared with control, whereas ORs >1 represent increased odds of self-harm. SMDs <0 represent a reduction in general psychopathology, depression, and suicidal ideation symptoms in the intervention compared with control, whereas SMDs >0 represent increased symptoms. Where outcomes or baseline moderators comprised continuous data from different scales, scores were standardized in each study and time period. This was done using the mean and pooled SD, applying an approximate Hedges' g adjustment, before conducting the meta-analysis. Further details of analysis and changes from the protocol are in Supplement 2, available online.

Pooled Treatment Effects

We used a 2-step approach,[26] estimating treatment effects in each study separately, then pooling aggregate results. Step 1 (SAS 9.4[23]) used logistic, linear, and Cox proportional hazards regression, adjusted for age (continuous) and sex at birth as appropriate to the outcome. To address the bias caused by rare events in logistic regression, Firth's penalized likelihood[27] was applied. Analyses accounted for cluster randomization using multilevel mixed-effects regression with a random cluster effect. Step 2 (STATA 17[24]) used random-effects meta-analysis allowing for statistical heterogeneity (variability in the intervention effects between studies being evaluated), which may be explained by clinical and methodological diversity of studies. Estimation used restricted maximum likelihood,[28] and CIs were derived using the Hartung-Knapp-Sidik-Jonkmann[29] approach to allow for uncertainty in variance estimates. CIs are also provided without the Hartung-Knapp-Sidik-Jonkmann adjustment to support comparison with previous meta-analyses for the primary outcome and secondary outcomes at the primary 12-month time point.

We report estimated pooled treatment effects, 95% CIs, and 95% prediction intervals alongside forest plots with study-specific treatment effect estimates. Statistical heterogeneity, indicating inconsistent treatment effects, was assessed using τ^2 (indicating the variability of true effect sizes under a random-effects model) and I^2 (representing the proportion of total variability due to between-study heterogeneity) with Cochran Q test assessed using $p < .1$ rather than $p < .05$, as it is widely accepted that the test has poor power when there are few studies.

Secondary analysis incorporated available published AD[30] for studies where IPD were not available. Here, IPD were reduced to AD in step 1 without adjustment for baseline covariates, and estimates were combined with existing AD from studies without IPD. Sensitivity analyses were conducted to test the robustness of our conclusions to our analysis methods by imputing missing IPD using multiple imputation, undertaking single-stage IPD meta-

analysis, and excluding studies of high risk of bias (for the primary outcome).

Moderating Study and Treatment-Level Effects

Random-effects subgroup analysis (categorical variables) and meta-regression (continuous variables) were used to explore sources of between-study heterogeneity on treatment effect estimates and specifically the impact of clinical diversity in participant populations, intervention delivery, and methodological diversity of study conduct and design. We used 2-stage IPD+AD meta-analyses to maximize the number of studies included. Analysis was conducted separately for each moderator across all interventions (due to limited numbers of studies for each intervention). To minimize the potential for spurious findings, analyses were conducted on the primary outcome only and repeated using secondary outcomes only if evidence of moderating effects was detected to ensure consistent findings across outcomes. Candidate moderators were the following:

- Full vs partial sample eligible
- Pilot/feasibility vs effectiveness design
- Study sample size powered vs not
- United States vs other (differences in self-harm definition)
- Low risk of bias vs some concerns vs high
- Self-report data/researcher interview vs hospital/medical records
- Control TAU/standard care/assessment vs enhanced TAU/good clinical care vs active
- Group element to intervention
- Family element to intervention
- Low, medium, high intervention intensity
- Years since primary publication
- Number of eligible participants
- Planned treatment duration
- Number of planned treatment sessions

Moderating Adolescent-Level Effects

We examined whether treatment effects remained uniform across adolescent moderators. Analyses of predetermined key moderators were conducted on primary and secondary outcomes. Additional moderator analyses were performed on the primary outcome only if the potential moderator was documented in at least half of the trials. These analyses were extended to secondary outcomes only when subgroup effects were observed on the primary outcome, to verify consistency across different outcomes. Results for primary and secondary outcomes related to self-harm repetition are presented together to facilitate comparison.

We used 2-stage IPD meta-analyses, extending the modeling approach for the primary analysis of pooled treatment effects. Each adolescent moderator was included as a fixed effect alongside a moderator-by-treatment interaction in step 1. Step 2 pooled the moderator-by-treatment interaction estimates, representing the change in the treatment effect for different levels of the moderator (ie, a 1-year increase in age, male vs female participants).[31] These analyses considered, but did not account for, cluster randomization[32] as no clustering effects were observed in the primary analysis of pooled treatment effects. We present CIs with and without this Hartung-Knapp-Sidik-Jonkmann adjustment in sensitivity analyses to aid hypothesis generation. Due to the exploratory nature of the analysis, prediction intervals were not calculated. We present forest plots displaying estimated pooled interaction effects and their 95% CIs alongside study-specific estimates and estimates by categorical moderators for easier understanding.

Data Availability Bias, Small Study Effects, and Publication Bias

We examined whether studies with and without IPD were systematically different by comparing study and participant baseline characteristics. We investigated small study effects and publication bias by inspecting funnel plots and via Egger's test assessed using $p < .1$ due to low power.[33] For potential asymmetry, we report results of fixed single-stage IPD meta-analysis (sensitivity analysis) in which less weight is given to smaller studies.

Data Sharing

Individual-level data cannot be made available to others due to confidentiality agreements in the original studies.

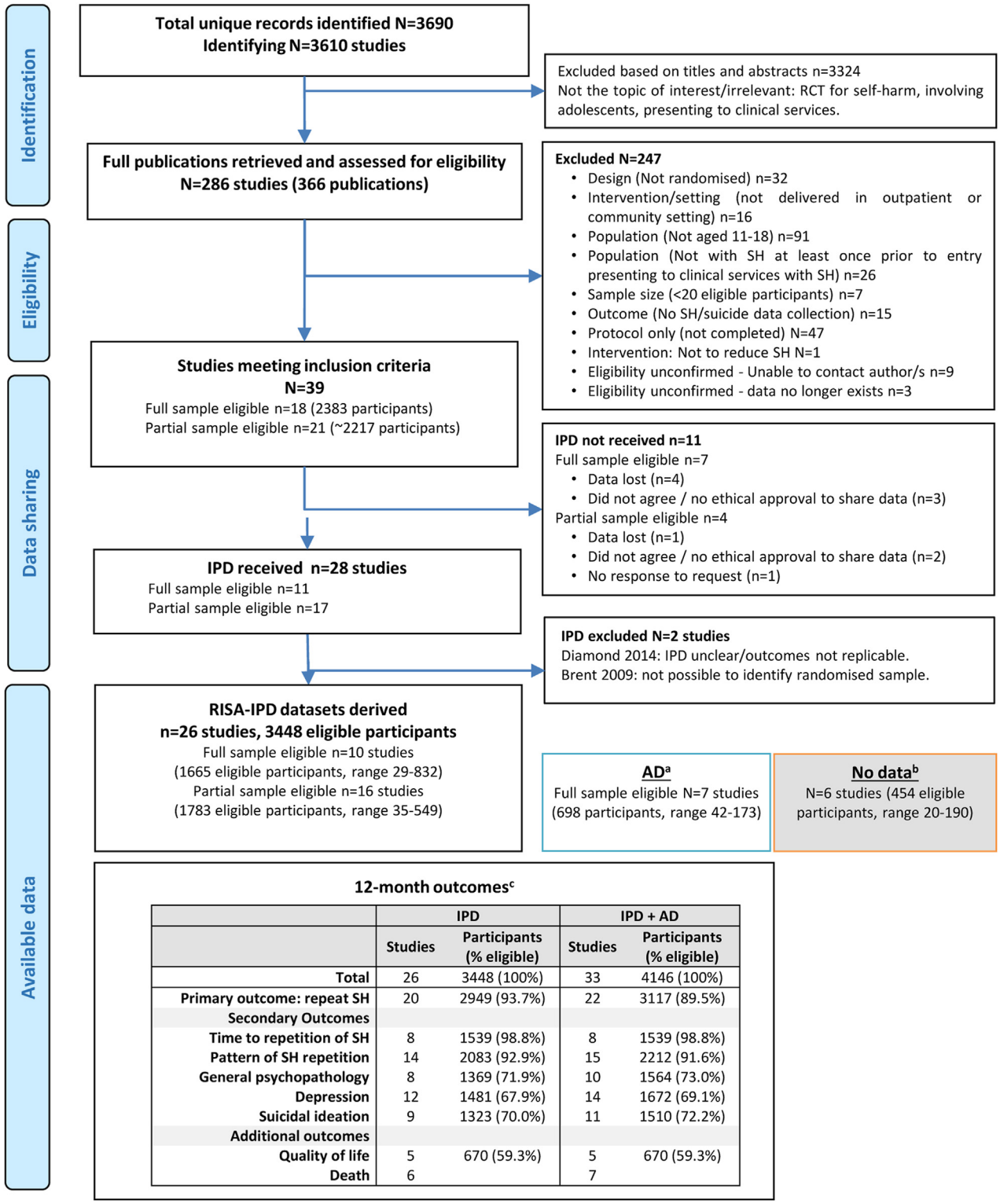
RESULTS

Detailed results are provided for data availability, derivations, and IPD integrity in Supplement 3, available online. Additional tables and figures associated with overall pooled results are in Supplement 4, available online. Participant moderators are provided in Supplement 5, available online. Tables of all meta-analysis results are in Supplement 6, available online.

Selected Studies

Up to January 21, 2022, we screened 3,690 citations and 286 full texts to identify studies. We sought IPD for 4,600 participants from 39 eligible studies (2,383 participants from 18 full sample eligible studies; 2,217 participants from 21 partial sample eligible studies) (Figure 1). We obtained

FIGURE 1 PRISMA Flowchart



12-month outcomes[c]

	IPD		IPD + AD	
	Studies	Participants (% eligible)	Studies	Participants (% eligible)
Total	26	3448 (100%)	33	4146 (100%)
Primary outcome: repeat SH	20	2949 (93.7%)	22	3117 (89.5%)
Secondary Outcomes				
Time to repetition of SH	8	1539 (98.8%)	8	1539 (98.8%)
Pattern of SH repetition	14	2083 (92.9%)	15	2212 (91.6%)
General psychopathology	8	1369 (71.9%)	10	1564 (73.0%)
Depression	12	1481 (67.9%)	14	1672 (69.1%)
Suicidal ideation	9	1323 (70.0%)	11	1510 (72.2%)
Additional outcomes				
Quality of life	5	670 (59.3%)	5	670 (59.3%)
Death	6		7	

Note: *AD = aggregate data; IPD = individual participant data; RCT = randomized controlled trial; RISA-IPD = Reducing Self-harm in Adolescents: Individual Participant Data meta-analysis. [a]Studies where published summary statistics were available for inclusion in the meta-analysis (ie, for studies in which the full sample were eligible for RISA-IPD). [b]Studies where no data were available for inclusion in the meta-analysis as reliable published statistics were not available for the RISA-IPD eligible sample of participants. [c]IPD and AD available, for 26 and 7 studies, respectively, included data on a range of outcomes and time points; therefore the number of studies with data available at the primary 12-month time point represents a subset of all studies with data available.*

IPD from 26 (66.7%) studies including 3,448 (75.0%) participants and further AD from 7 (17.9%) studies including 698 (15.2%) participants. Data were missing for 6 (15.4%) studies and 454 (9.9%) participants.[18] One study provided IPD, but repetition of self-harm outcomes were unavailable.

Study Characteristics and Risk of Bias

Tables 1 and 2 detail and summarize eligible study characteristics (see also [18]). Studies were conducted across a wide range of countries and interventions, with the largest proportion in the United States (38.5%). Of eligible studies, CBT was evaluated in 10 studies (25.6%, 7 with IPD), PST in 6 studies (15.4%, 5 with IPD), family therapy and postcards/tokens in 5 studies (12.8%, 3 with IPD), DBT in 4 studies (10.3%, 2 with IPD), CAT/MBT in 3 studies (7.7%, all with IPD), group therapy in 3 studies (7.7%, 2 with IPD), brief intervention in 2 studies (5.1%, 1 with IPD), and multisystemic therapy in 1 study (2.6%, no IPD). Slightly more than half of the eligible studies evaluated interventions of medium intensity, whereas 8 (20.5%) evaluated low-intensity interventions and 10 (25.6%) evaluated high-intensity interventions. Controls predominantly consisted of TAU in 25 eligible studies (64.1%, 18 with IPD), enhanced TAU in 8 (20.5%, 5 with IPD), and active intervention in 6 (15.4%, 3 with IPD). Outcomes were most commonly reported at 3, 6, and 12 months after randomization. Further details can be found in Cottrell *et al.*[18]

Risk of bias for studies providing IPD on repetition of self-harm outcomes was rated as low risk, some concerns, and high risk for 6 of 25 (24%), 16 of 25 (64%), and 3 of 25 (12%) studies. Additional AD were available for 5 studies with some concerns and 2 with high risk. No data were available for 4 studies with some concerns and 3 with high risk. The number of studies with concerns or high risk largely arose from outcomes being self-reported from non-blinded participants and studies not having prespecified published analysis plans.[18]

Available Adolescent-Level Moderators

Age and gender were the only baseline characteristics available in all 26 studies with IPD (Table 3). Most participants were female (2,823/3,448, 82.0%) with mean (SD) age 15.7 (1.6) years. In 14 (53.8%) studies with IPD, 1,471 of 2,779 (52.9%) participants presented to services with self-poisoning, 1,052 (37.9%) presented with self-injury, and 245 (8.8%) presented with a combination. In 5 of these studies, the majority or all participants had presented with self-poisoning. In 7 (26.9%) studies, including all 3 studies of CAT/MBT, 163 of 921 (17.7%) participants identified as having borderline personality disorder. More than half of the participants were reported as depressed (1,138/1,989 [57.2%]; 15 studies) and had engaged in self-harm multiple times (1,874/3,213 [59.3%]; 21 studies). Slightly more than half of the participants had anxiety (clinically diagnosed or indicated based on questionnaire; 917/1,682 [54.5%]; 14 studies). More than three-fourths of participants were White (1,947/2,482 [78.4%]; 18 studies). Slightly less than three-fourths exhibited suicidal ideation (1,620/2,221 [72.9%]; 15 studies); in 1 study, all participants showed suicidal ideation as it was a criterion for eligibility. Family dysfunction was indicated in 747 of 966 participants (77.3%; 4 studies), and 325 of 2,198 participants (14.8%; 12 studies) were on psychotropic medication at baseline. Whereas data were available in less than half the trials, these were included in analyses as additional moderators as available in all 3 family therapy studies. Other baseline characteristics available in fewer than half of the studies included unemotional and callous traits, LGBTQ (lesbian, gay, bisexual, transgender, and queer) status, autistic spectrum disorder, abuse, presence of an eating disorder, intellectual disability, out-of-home placement, and presence of a physical health problem. See Supplement 3, available online, for further details.

Primary Outcome—Repetition of Self-harm

Overall, 2,949 (93.7% eligible) participants from 20 studies and 3,117 (89.5% eligible) participants from 22 studies were included in IPD and IPD+AD meta-analyses, respectively, at 12 months (Figure 2, Table 4), of whom 973 (33.0%) and 995 (31.9%) participants were reported to have engaged in repeat self-harm, with repetition rates ranging from 6.1% to 92.3% (Supplement 4, Table S4.2.2, available online). There was no evidence that interventions were more or less effective than controls at reducing repeat self-harm at 12 months using IPD (odds ratio [OR] 1.06 [95% CI 0.86, 1.31], 20 studies, 2,949 participants) or IPD+AD (OR 1.02 [95% CI 0.82, 1.27], 22 studies, 3,117 participants) or at other time points. Whereas the CIs include the null effect, the upper and lower bounds include both small positive and negative adverse effects. Due to high levels of within-study variability in outcome, between-study heterogeneity in treatment effects was relatively low (IPD: $I^2 = 1.1\%$, $p = .443$; IPD+AD: $I^2 = 12.1\%$, $p = .299$), and there was no evidence of heterogeneity in treatment effects between groups of interventions (IPD: $p = .779$; IPD+AD: $p = .759$) (ie, intervention-specific effects were consistent, and did not differ significantly) across studies.

TABLE 1 Characteristics of Included Studies

First author, year	Data available[a]	Country	Design	Aim[b]	Study powered	Total sample size (eligible)	Eligibility	Mean age, y	% Female participants
Asarnow, 2011[34]	No data	United States	2-arm RCT	Effectiveness	Yes	181	Partial	14.7	69
Asarnow, 2017[35]	Aggregate	United States	2-arm RCT	Pilot	No	42	Full	14.6	88.1
Brent, 2009[36]	No data	United States	3-arm RCT/preference	Pilot	No	124 (22 randomized)	Partial	15.7	77.4
Carter, 2007[37]	IPD	Australia	2-arm Zelen RCT	Effectiveness	Yes	772 (68 ages 11-18)	Partial	17.6	82.4
Chanen, 2008[38]	IPD	Australia	2-arm RCT	Effectiveness	Yes	86 (72 prior SH)	Partial	16.4	79.2
Cooney, 2010[39]	IPD	New Zealand	2-arm RCT	Pilot	No	29	Full	16	75.9
Cotgrove, 1995[40]	Aggregate	United Kingdom	2-arm RCT	Effectiveness	No	105	Full	14.9	84.8
Cottrell, 2018[41]	IPD	United Kingdom	2-arm RCT	Effectiveness	Yes	832	Full	14.8	88.6
Diamond, 2010[42]	IPD	United States	2-arm RCT	Effectiveness	No	66 (41 prior SH)	Partial	15	92.7
Diamond, 2014[e]	No data	United States	2-arm RCT	Pilot	No	20	Full	14.9	80
Diamond, 2019[43]	IPD	United States	2-arm RCT	Effectiveness	Yes	129 (90 with prior SH)	Partial	15	84.4
Donaldson, 2005[44]	IPD	United States	2-arm RCT	Pilot	No	44[f]	Full	14.9	79.5
Esposito-Smythers, 2011[45]	IPD	United States	2-arm RCT	Pilot	No	40 (35 prior SH)	Partial	15.7	65.7
Esposito-Smythers, 2017[46]	IPD	United States	2-arm RCT	Pilot	No	81 (37 prior SH)	Partial	15.5	67.6
Esposito-Smythers, 2019[47]	IPD	United States	2-arm RCT	Effectiveness	Yes	147 (133 prior SH)	Partial	14.8	79.7
Green, 2011[48]	IPD	United Kingdom	2-arm RCT	Effectiveness	Yes	366	Full	15.1	88.5
Griffiths, 2019[49]	IPD	United Kingdom	2-arm RCT	Pilot	No	53	Full	15.5	79.2
Hassanian-Moghaddam, 2017[50]	IPD	Iran	2-arm RCT	Effectiveness	Yes	2,300 (549 age 11-18)	Partial	16.7	74.3
Harrington, 1998[51]	Aggregate	United Kingdom	2-arm RCT	Effectiveness	Yes	162	Full	14.5	89.5
Hatcher, 2011[52]	IPD	New Zealand	2-arm Zelen RCT	Effectiveness	Yes	1,094 (89 ages 11-18)	Partial	18.3	67.4
Hatcher, 2015[53]	IPD	New Zealand	2-arm Zelen RCT	Effectiveness	Yes	1,474 (98 ages 11-18)	Partial	17.8	77.6
Hazell, 2009[54]	IPD	Australia	2-arm RCT	Effectiveness	No	82	Full	14.5	90.2
Huey, 2004[55]	No data	United States	2-arm RCT	Effectiveness	No	156 (70 with prior SH)	Partial	12.9	35
Husain, 2014[56]	IPD	Pakistan	2-arm RCT	Effectiveness	Yes	221 (53 ages 11-18)	Partial	17.4	77.4
Kaess, 2020[57]	IPD	Germany	2-arm RCT	Effectiveness	Yes	74	Full	14.9	95.9
King, 2006[58]	No data	United States	2-arm RCT	Effectiveness	No	289 (190 prior SH)	Partial	15.3	68.2
King, 2009[59]	IPD	United States	2-arm RCT	Effectiveness	No	448 (331 prior SH)	Partial	15.6	73.1
McCauley, 2018[60]	Aggregate	United States	2-arm RCT	Effectiveness	Yes	173	Full	14.9	94.8
Mehlum, 2014[61]	Aggregate	Norway	2-arm RCT	Effectiveness	Yes	77	Full	15.6	88.3
Morthorst, 2012[62]	IPD	Denmark	2-arm RCT	Effectiveness	Yes	243 (46 ages 11-18)	Partial	16.1	95.7
O'Connor, 2017[63]	IPD	United Kingdom	2-arm RCT	Effectiveness	Yes	518 (39 ages 11-18)	Partial	17.2	74.4
Ougrin, 2013[32]	IPD	United Kingdom	2-arm cluster RCT	Effectiveness	Yes	70	Full	15.6	80
Pineda, 2013[64]	IPD	Australia	2-arm RCT	Effectiveness	Yes	48 (48 with prior SH[g])	Partial	15.1	79.2
Robinson, 2012[65]	No data	Australia	2-arm RCT	Effectiveness	Yes	164 (~56 ages 11-18 prior SH)	Partial	18.6	64.6
Rossouw, 2012[66]	IPD	United Kingdom	2-arm RCT	Effectiveness	Yes	80	Full	15.1	85
Santamarina-Perez, 2017, 2020[67,68]	IPD	Spain	2-arm RCT	Effectiveness	No	35	Full	15.3	88.6
Spirito, 2002[69]	Aggregate	United States	2-arm RCT	Effectiveness	No	76	Full	15	90
Tyrer, 2003[70]	IPD	United Kingdom	2-arm RCT	Effectiveness	Yes	480 (54 ages 11-18)	Partial	17.8	88.9
Wood, 2001[71]	Aggregate	United Kingdom	2-arm RCT	Pilot	No	63	Full	14.2	78

Note: Active = active control; BAME = Black, Asian and minority ethnic; CALD = culturally and linguistically diverse; CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; E-TAU = enhanced treatment as usual; IPD = individual participant data; MST = multisystemic therapy; NESB = non–English-speaking background; Postcards/tokens = postcards, tokens, documents; PST = problem solving, psychoeducation, support; RCT = randomized controlled trial; RISA = Reducing Self-harm in Adolescents; SH = self-harm; TAU = treatment as usual.

[a]*The reasons IPD were not provided or excluded were: the data had been lost and were no longer available for Cotgrove, 1995,[40] Harrington, 1998,[51] Spirito, 2002,[69] Wood, 2001,[71] and King, 2009[59]; authors did not agree to share data or felt they did not have ethical approval to share for Asarnow, 2011,[34] Asarnow, 2017,[35] McCauley, 2018,[60] Mehlum, 2014,[61] and Robinson, 2012[65]; there was no response to our request for Huey, 2004[55]; IPD were obtained but excluded for Diamond, 2014 (unpublished data) as the IPD were not consistent with limited aggregate results detailed in the list of excluded studies in Hawton 2015[72]; and IPD were obtained but excluded for Brent, 2009[36] as eligible participants could not be identified.*

[b]*Pilot studies include pilot or feasibility studies.*

[c]*Ethnicity as reported in original studies, with the exception of Santamarina, 2020[67,68] as based on IPD; Caucasian as reported in King, 2009.[59]*

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

[e]*Unpublished data; ClinicalTrials.gov NCT01195740.*

[f]*Donaldson, 2005[44] reported 39 randomized, but IPD confirmed 44 randomized.*

[g]*Pineda, 2013[64]: Partially eligible as eligibility based on suicidal behavior including ideation only; however, the authors confirmed all met RISA eligibility criteria. IPD did not include the RISA primary outcome (aggregate data also unavailable).*

TABLE 1 Continued

% Race/ethnicity[c]	Intervention	Control group	Treatment intensity	Treatment duration, wk	No. treatment sessions	Any group element in treatment	Any family element in treatment	Method of self-harm data collection[d]	Overall risk of bias
African American, 13; Hispanic, 45; other, 9; White non-Hispanic, 33	CBT	TAU	Low	4	5	No	Yes	Self-report	Some concerns
African American, 5; Asian, 12; Hispanic/Latino, 21; other, 7; White non-Hispanic, 83	CBT	E-TAU	Medium	12	10	No	Yes	Self-report	Some concerns
Not possible to determine for randomized	CBT	Active	High	26	24	No	Yes	Self-report	High
Not reported	Postcards/tokens	TAU	Low	52	0	No	No	Medical records	High
Not reported	CAT/MBT	E-TAU	High	24	24	No	No	Self-report	Some concerns
New Zealand European, 77; New Zealand Māori, 3; other European, 3; South African, 7; United Kingdom 10	DBT	TAU	High	26	52	Yes	Yes	Self-report	High
Not reported	Postcards/tokens	TAU	Low	0	0	No	No	Medical records	High
Asian, 3; Black, 7; other ethnic group, 5; White, 84; missing <1	Family therapy	TAU	Medium	26	8	No	Yes	Medical records	Low
African American, 74	Family therapy	E-TAU	Medium	12	12	No	Yes	Self-report	Some concerns
African American, 65	Family therapy	E-TAU	—	16	16	No	Yes	Self-report	High
African American, 50; American Indian/Alaska Native, 2; Asian, 2; Hispanic, 16; multiracial, 8; Native Hawaiian/Pacific Islander, 1; other, 9; White, 29%	Family therapy	Active	Medium	16	16	No	Yes	Self-report	Some concerns
African American, 5%; Hispanic, 10; White, 85%	PST	Active	Medium	26	10	No	Yes	Self-report	High
Race: White, 89; ethnicity: Hispanic, 14	CBT	E-TAU	High	52	54	No	Yes	Self-report	Some concerns
Race: Black, 37; other, 20; White, 42; ethnicity: Hispanic, 17	CBT	E-TAU	Medium	4	3	Yes	Yes	Self-report	Some concerns
Race: Asian/Pacific Islander, 3; Black/African American, 2; multiracial, 1; White, 86; Ethnicity: non-Hispanic/Latino, 83	CBT	E-TAU	High	52	54	No	Yes	Combined approach	Low
BAME, 6	Group therapy	TAU	Medium	6	10	Yes	No	Self-report	Some concerns
White/Scottish, 69	CAT/MBT	TAU	Medium	12	12	Yes	No	Medical records	Some concerns
Not reported	Postcards/tokens	TAU	Low	12	0	No	No	Self-report	Some concerns
Not reported	Family therapy	TAU	Medium	—	5	No	Yes	Self-report	Some concerns
Asian, 3; Māori, 16; New Zealand European, 61; other, 14; Pacific Islander, 6	CBT	TAU	Medium	12	9	No	No	Medical records	Low
Asian, 6; Māori 7; New Zealand European, 79; other, 2; Pacific Islander, 7	CBT	TAU	Medium	52	8	No	No	Medical records	Low
Not reported	Group therapy	TAU	Medium	6	6	Yes	No	Self-report	Some concerns
African American, 65; European American, 33; other, 1	MST	Active	High	16	—	No	Yes	Self-report	Some concerns
Not reported	PST	TAU	Medium	12	6	No	No	Self-report	Some concerns
Migration status: Germany, 92	CBT	TAU	Medium	16	12	No	No	Self-report	Some concerns
Black, 10; other, 7; White, 82	PST	TAU	Medium	26	26	No	Yes	Self-report	Some concerns
African American, 6; Caucasian, 84; Hispanic, 2; other, 8	PST	TAU	Medium	12	12	No	Yes	Self-report	Some concerns
African American, 7; Asian American, 6; Hispanic, 27; Native American, <1; other, 2; White, 56	DBT	Active	High	26	52	Yes	Yes	Self-report	Some concerns
Norwegian ethnicity, 85	DBT	E-TAU	High	19	38	Yes	Yes	Medical records	Some concerns
Danish, 67; European/American, 8; Middle Eastern, 14; other, 10	PST	TAU	Medium	26	20	No	Yes	Medical records	Some concerns
Not reported	Postcards/tokens	TAU	Low	8	1	No	No	Medical records	Low
Asian, 11; Black, 20; mixed, 13; other, 3; White, 53	Brief intervention	TAU	Low	1	1	No	Yes	Medical records	Some concerns
Aboriginal 8; Anglo-Saxon, 58; CALD/NESB, 35	PST	TAU	Medium	8	4	No	Yes	Self-report	Some concerns
Born in Australia, 89	Postcards/tokens	TAU	Low	52	0	No	No	Self-report	High
Asian, 10; Black, 5; mixed, 7.5; other, 2.5; White, 75	CAT/MBT	TAU	High	52	64	No	Yes	Self-report	Some concerns
White, 91	DBT	Active	High	16	40	Yes	Yes	Combined approach	Some concerns
African American, 11; Hispanic, 13; mixed ancestry, 3; White, 73	Brief intervention	TAU	Low	8	5	No	Yes	Self-report	High
White, 90	CBT	TAU	Medium	12	7	No	No	Combined approach	Low
Not reported	Group therapy	TAU	Medium	26	26	Yes	No	Self-report	Some concerns

Except CBT at 12 months, most intervention-specific pooled effect estimates were based on 4 or fewer studies. There was no evidence that any were more or less effective than control at reducing repeat self-harm at any time period in primary IPD or IPD+AD meta-analysis. There was evidence of between-study heterogeneity in treatment effects at the 10% level for the 2 or 3 studies of group therapy (IPD: $I^2 = 72.2\%$, p = .058; IPD+AD: $I^2 = 76.2\%$, $p = .015$) at 12 months and between 2 IPD studies of CBT at 18 months ($I^2 = 71.7\%$, $p = .06$) and CAT/MBT at 3 months ($I^2 = 64.6\%$, $p = .093$) in which contrasting treatment effects were observed.

Funnel plots showed no evidence of small study effects or publication bias. There were few notable differences in results and no changes to conclusions from sensitivity analyses using multiple imputation, 1-stage random- or fixed-effects IPD meta-analysis or IPD+AD meta-analysis excluding studies of high risk of bias. Compared with random-effects analysis, 1-stage fixed-effects IPD meta-analysis provided similar estimates but with tighter CIs.

TABLE 2 Study Characteristics by Data Availability

	IPD (n = 26)		AD (n = 7)		No data (n = 6)		Total (n = 39)	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Eligibility								
Full sample eligible	10	(38.5)	7	(100.0)	1	(16.7)	18	(46.2)
Partial eligible	16	(61.5)	0	(0.0)	5	(83.3)	21	(53.8)
No. eligible participants								
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
	132.6	(187.54)	99.7	(50.06)	75.7	(63.06)	117.9	(156.68)
	Median	**(range)**	**Median**	**(range)**	**Median**	**(range)**	**Median**	**(range)**
	69.0	(29, 832)	77.0	(42, 173)	63.0	(20, 190)	70.0	(20, 832)
	Total	**Total**	**Total**	**Total**				
	3,448	698	454	4,600				
Age, y[a]								
	Weighted mean	**(SD)**	**Weighted mean**	**(SD)**	**Weighted mean**	**(SD)**	**Weighted mean**	**(SD)**
	15.7	(1.6)	14.8	(—)	15.4	(—)	15.5	(—)
	Range of study means		**Range of study means**		**Range of study means**		**Range of study means**	
	14.5, 18.3		14.2, 15.6		12.9, 18.6		12.9, 18.6	
% Female participants[b]								
	Weighted mean		**Weighted mean**		**Weighted mean**		**Weighted mean**	
	82.0		88.9		63.7		79.6	
	Range of study means		**Range of study means**		**Range of study means**		**Range of study means**	
	65.7, 95.9		78.0, 94.8		35.0, 80.0		35.0, 95.9	
Years since primary publication								
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
	9.3	(4.79)	15.3	(9.89)	12.7	(3.78)	10.9	(6.18)
	Median	**(range)**	**Median**	**(range)**	**Median**	**(range)**	**Median**	**(range)**
	10.0	(2.0, 19.0)	20.0	(4.0, 27.0)	12.0	(8.0, 18.0)	11.0	(2.0, 27.0)
Country[c]								
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
United States	7	(26.9)	3	(42.9)	5	(83.3)	15	(38.5)
Rest of world	19	(73.1)	4	(57.1)	1	(16.7)	24	(61.5)
Pilot/feasibility or effectiveness trial								
Pilot/feasibility	5	(19.2)	2	(28.6)	2	(33.3)	9	(23.1)
Effectiveness	21	(80.8)	5	(71.4)	4	(66.7)	30	(76.9)
Study powered								
No	9	(34.6)	4	(57.1)	4	(66.7)	17	(43.6)
Yes	17	(65.4)	3	(42.9)	2	(33.3)	22	(56.4)
RISA intervention								
CBT	7	(26.9)	1	(14.3)	2	(33.3)	10	(25.6)
DBT	2	(7.7)	2	(28.6)	0	(0.0)	4	(10.3)
Family therapy	3	(11.5)	1	(14.3)	1	(16.7)	5	(12.8)
Group therapy	2	(7.7)	1	(14.3)	0	(0.0)	3	(7.7)
CAT/MBT	3	(11.5)	0	(0.0)	0	(0.0)	3	(7.7)
MST	0	(0.0)	0	(0.0)	1	(16.7)	1	(2.6)
PST	5	(19.2)	0	(0.0)	1	(16.7)	6	(15.4)
Postcards/tokens	3	(11.5)	1	(14.3)	1	(16.7)	5	(12.8)
Brief intervention	1	(3.8)	1	(3.8)	0	(0.0)	2	(5.1)
RISA control group[d]								
TAU	18	(69.2)	4	(57.1)	3	(50.0)	25	(64.1)

(continued)

TABLE 2 Continued

	IPD (n = 26)		AD (n = 7)		No data (n = 6)		Total (n = 39)	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
E-TAU	5	(19.2)	2	(28.6)	1	(16.7)	8	(20.5)
Active	3	(11.5)	1	(14.3)	2	(33.3)	6	(15.4)
Treatment intensity								
Low	4	(15.4)	2	(28.6)	2	(33.3)	8	(20.5)
Medium	16	(61.5)	3	(42.9)	1	(16.7)	20	(51.3)
High	6	(23.1)	2	(28.6)	2	(33.3)	10	(25.6)
Unknown	0	(0.0)	0	(0.0)	1	(16.7)	1	(2.6)
Treatment duration, wk								
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
	21.3	(16.77)	15.2	(10.40)	23.3	(16.23)	20.6	(15.70)
	Median	**(range)**	**Median (range)**	**(range)**	**Median (range)**	**(range)**	**Median (range)**	**(range)**
	14.0	(1, 52)	15.5	(0, 26)	21.0	(4, 52)	16.0	(0, 52)
No. treatment sessions								
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**
	17.1	(18.95)	19.4	(19.71)	14.2	(11.45)	17.2	(17.95)
	Median	**(range)**	**Median**	**(range)**	**Median**	**(range)**	**Median**	**(range)**
	10.0	(0, 64)	10.0	(0, 52)	16.0	(0, 26)	10.0	(0, 64)
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Group element in treatment, yes	6	(23.1)	3	(42.9)	0	(0.0)	9	(23.1)
Family element in treatment, yes	14	(53.8)	5	(71.4)	5	(71.4)	24	(61.5)
Method of data collection: self-harm								
Self-report/researcher interview	15	(57.7)	5	(71.4)	6	(100.0)	26	(66.7)
Hospital/medical records	8	(30.8)	2	(28.6)	0	(0.0)	10	(25.6)
Combined approach	3	(11.5)	0	(0.0)	0	(0.0)	3	(7.7)
Overall risk of bias on the primary outcome								
Low	6	(23.1)	0	(0.0)	0	(0.0)	6	(15.4)
Some concerns	17	(65.4)	5	(71.4)	3	(50.0)	25	(64.1)
High	3	(11.5)	2	(28.6)	3	(50.0)	8	(20.5)

Note: AD = aggregate data; CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; E-TAU = enhanced treatment as usual; IPD = individual participant data; MST=multisystemic therapy; Postcards/tokens = postcards, tokens, documents; PST = problem solving, psychoeducation, support; RISA = Reducing Self-harm in Adolescents; TAU = treatment as usual.

[a]*For partially eligible studies with IPD, the mean age and % female participants is for the eligible sample; otherwise data are for the full recruited sample. Participants with IPD range in age from 11 to 18.9 years.*

[b]*Meta-regression based on primary outcome data collection self-report (including combined) vs medical records.*

[c]*Seven studies (26.9%) were conducted in the United States, 7 (26.9%) in Australasia, 7 (26.9%) in the United Kingdom, 3 (11.5%) elsewhere in Europe, and 2 (7.7%) in Asia. Additional AD for 7 studies included 3 studies in the United States, 3 studies in the United Kingdom, and 1 study in Norway.*

[d]*Active controls included antidepressant pharmacotherapy, family-enhanced nondirective supportive therapy, supportive relationship treatment, hospitalization, individual and group supportive therapy, and TAU + group session. E-TAU was described as such in original articles and also included standardized good clinical care and intensive TAU.*

Heterogeneity and Study-Level Moderating Effects. There was no statistical evidence of between-study heterogeneity in treatment effect when all interventions were compared with control at any time point. In IPD+AD meta-analyses, heterogeneity was estimated to be zero at all time points except for 12 months (I^2 = 12.1% [95% CI 0, 48.2%], 22 studies) and 18 months (I^2 = 14% [95% CI 0, 66.8%], 6 studies). Given the lack of heterogeneity and small number of studies, meta-regression was conducted only at 12 months. No candidate moderators were significantly associated with treatment effect (Figure 2).

TABLE 3 Summary of Participant Moderators in Studies With Individual Participant Data

Potential moderator	No. (%) studies with moderator available	Participants	Values	No. (%) participants[a]
Key moderators				
Age	26 (100)	3,437	Mean (SD)	15.7 (1.6)
Gender	26 (100)	3,448	Female	2,823 (81.9)
			Male	619 (18.0)
Depression (clinically indicated)	15 (57.7)	1,989	Clinical diagnosis	1,138 (57.2)
			No clinical diagnosis	771 (38.8)
Presenting self-harm method	14 (53.8)	2,779	Self-injury	1,052 (37.9)
			Self-poisoning	1,471 (52.9)
			Combined	245 (8.8)
Borderline personality disorder	7 (26.9)	921	Clinical diagnosis	163 (17.7)
			No clinical diagnosis	682 (74.0)
Additional and emerging moderators explored in meta-analyses				
No. previous self-harm episodes[b]	21 (80.8)	3,213	≤2	1,271 (39.6)
			Multiple	1,874 (59.3)
Anxiety disorder (clinical or questionnaire indicated)	14 (53.8)	1,682	Yes	917 (54.5)
			No	632 (37.6)
Family dysfunction	5 (19.2)[c]	966	Indicated	747 (77.3)
			Not indicated	205 (21.2)
Ethnicity	18 (69.2)	2,482	Black, Asian, other ethnicity	505 (20.3)
			White	1,947 (78.4)
Suicidal ideation	15 (57.7)	2,221	Indicated	1,620 (72.9)
			Not indicated	546 (24.6)
Psychotropic medication use	12 (46.2)[c]	2,198	Yes	325 (14.8)
			No	1,534 (69.8)
Additional and emerging moderators available in <~50% of studies or not included in further analysis				
Baseline self-harm outcome/ severity	18 (69.2)	2,643	NA, not possible to harmonize[d]	
Identify as LGBTQ	2 (7.7)	223	Yes	74 (33.2)
			No	121 (54.3)
Autism spectrum disorder	1 (3.8)	35	Indicated	0
			Not indicated	35 (100)
History of abuse (physical, sexual)	9 (34.6)	2,148	Yes	645 (30.0)
			No	1,379 (64.2)
Eating disorder	7 (26.9)	762	Yes	52 (6.8)
			No	508 (66.7)
Intellectual disability	3 (11.5)	985	Yes	55 (5.6)
			No	912 (92.6)
Out-of-home placement	9 (34.6)	2,394	Parents/guardians	2,056 (85.9)
			Foster care/other	236 (9.9)
Physical health problem	4 (15.4)	1,488	Yes	387 (26.0)
			No	1,098 (73.8)

Note: Additional continuous moderators not presented due to use of different scales, standardized before analysis: depression in 17 (65.4%) studies, family dysfunction in 5 (19.2%) studies, suicidal ideation score in 14 (53.8%) studies, unemotional/callous traits in 1 (3.8%) study. Study level summary is in Supplement 3, available online. LGBTQ = lesbian, gay, bisexual, transgender, and queer; NA = not applicable.

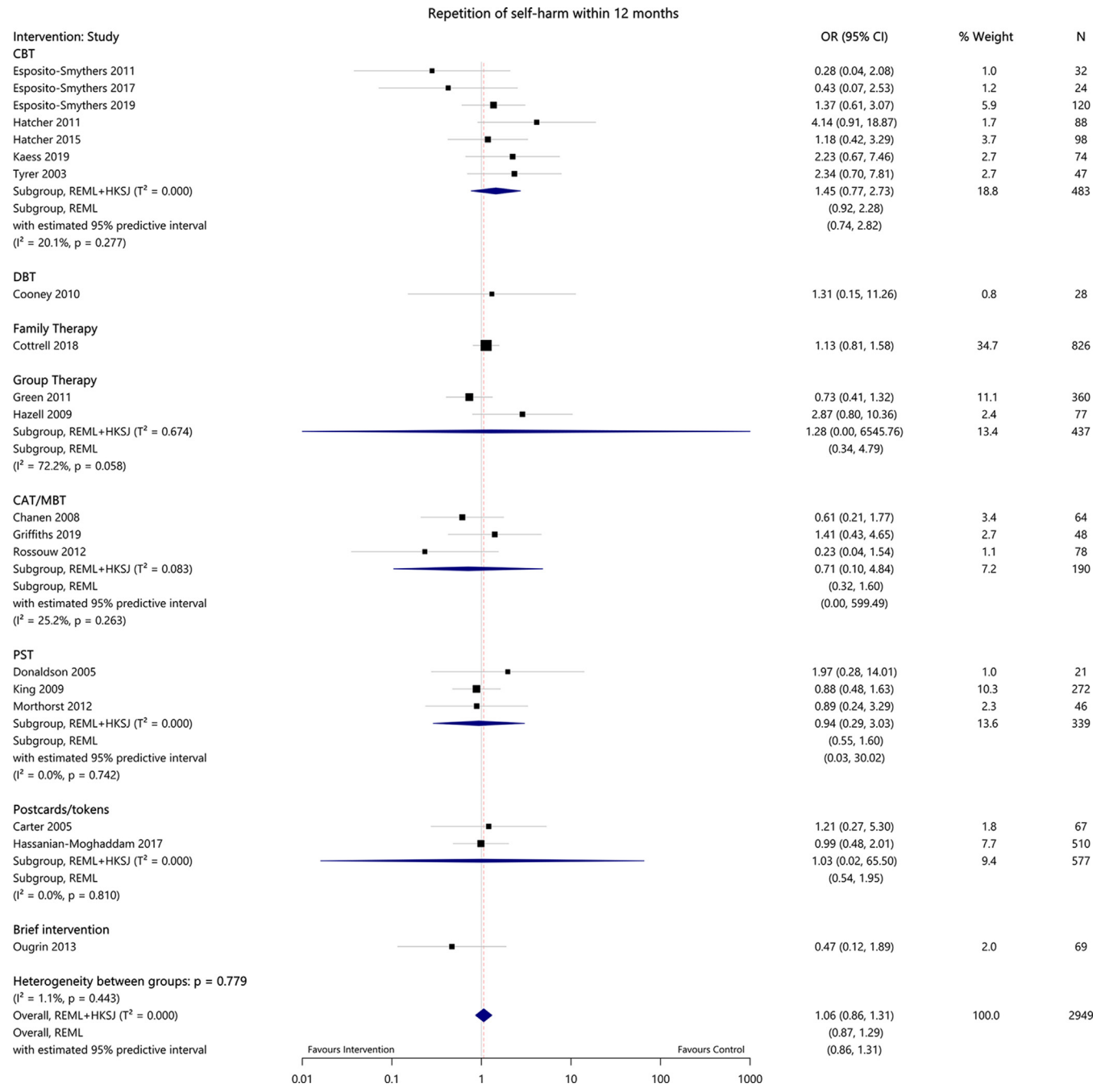
[a]*Unless otherwise indicated. Where % does not add to 100%, this is due to missing participant-level data.*

[b]*Due to variability in data collection methods within each study, we categorized the number of previous self-harm episodes as ≤2 or multiple for analysis (rather than 1, 2, or multiple episodes as had been planned) (Supplement 3, Table S3.16, available online).*

[c]*Included in analysis as present in 100% of family therapy studies.*

[d]*Due to considerable variability in data collection and definitions, further synthesis of these data was not carried out.*

FIGURE 2 Forest Plots of the Effect of Intervention vs Control on the Primary Outcome Self-harm (SH) Repetition at 12 Months

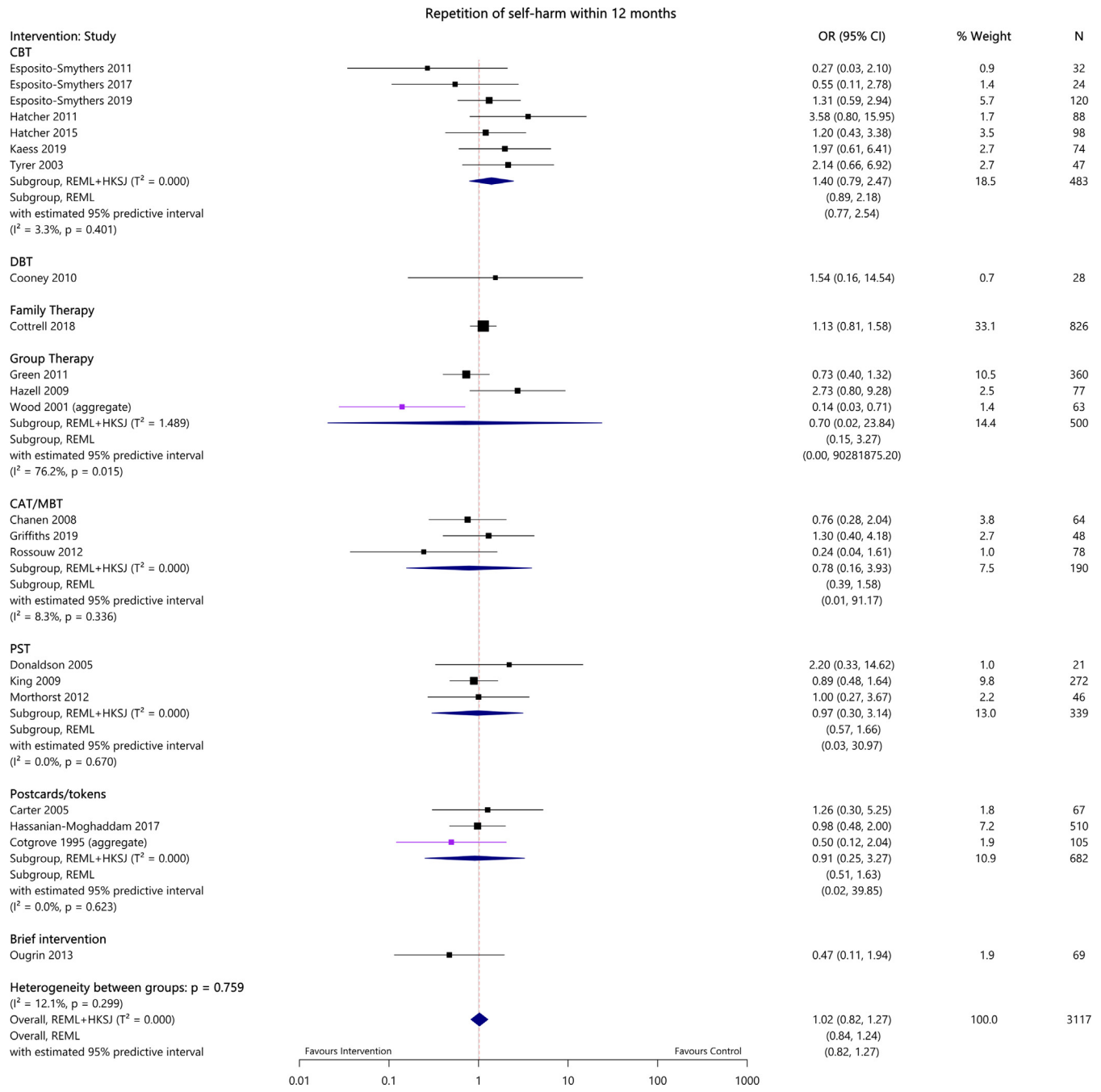


Note: *References to included studies can be found in Table 1, references 34-72. The first panel depicts adjusted individual participant data (IPD) meta-analysis. The second panel depicts unadjusted IPD and aggregate data (AD) meta-analysis. The third panel depicts unadjusted IPD and AD meta-regression. Purple color coding highlights studies where estimates are from AD. CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; HKSJ = Hartung-Knapp-Sidik-Jonkmann; OR = odds ratio; Postcards/tokens = postcards, tokens, documents; PST = problem solving, psychoeducation, support; REML = restricted maximum likelihood; TAU = treatment as usual. Please note color figures are available online.*

Secondary Outcomes

Time to Repetition of Self-harm. Overall, 1,539 (98.8% eligible) participants (8 studies) were included in IPD meta-analyses (Table 2; Supplement 4, Figure S4.4.1, available online). Median follow-up was 43 months (range 0-82.5 months) and ranged from 6 to 60 months across studies.

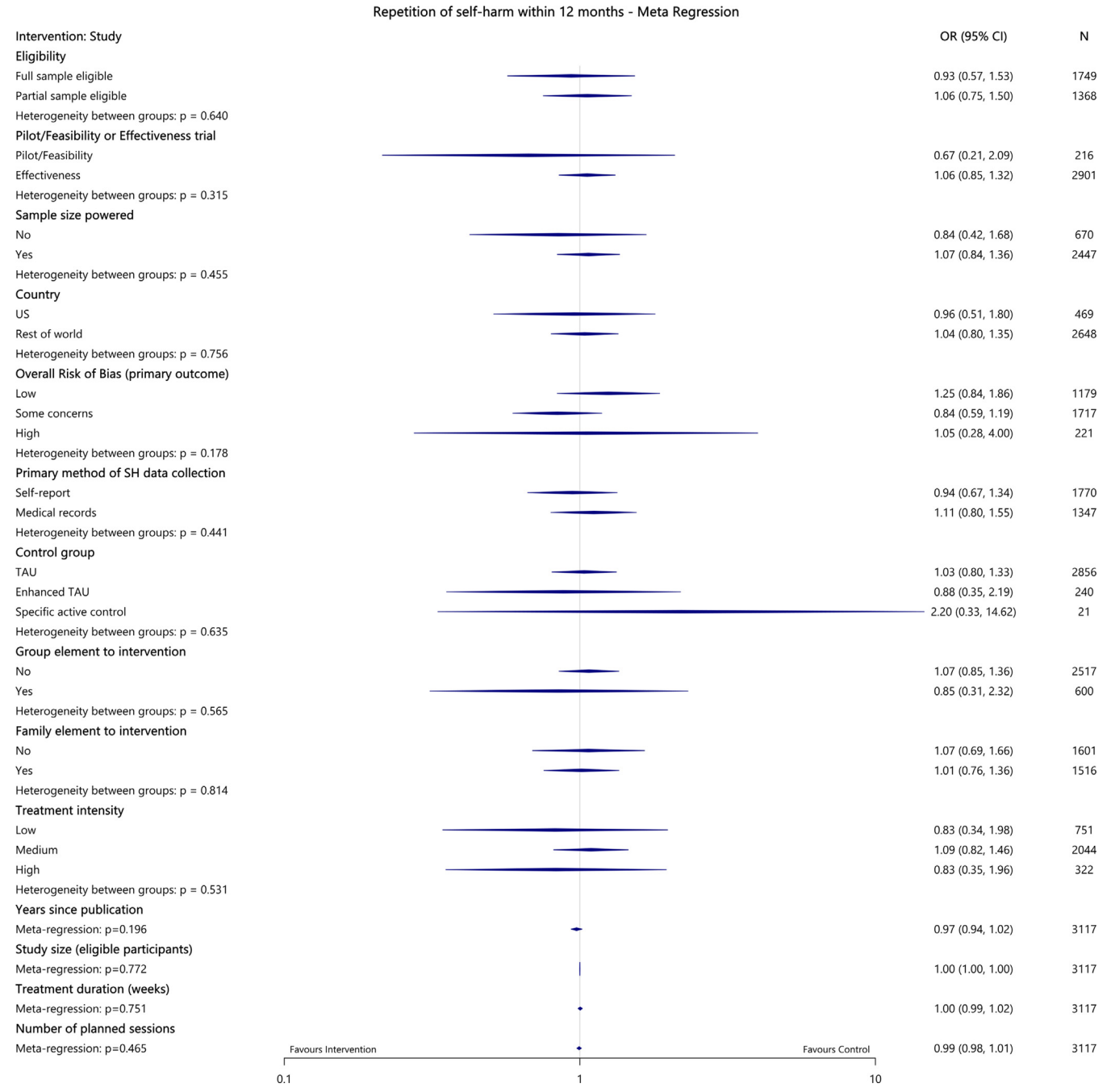
FIGURE 2 Continued



There was no evidence that interventions (overall or by intervention) were more or less effective than control on time to repetition in IPD meta-analyses. There was no evidence of between-study heterogeneity overall or by intervention or heterogeneity between groups of interventions.

Pattern of Self-harm Repetition. Overall, 2,083 (92.9% eligible) participants (14 studies) and 2,212 (91.6% eligible) participants (15 studies) were included in IPD and IPD+AD meta-analyses of self-harm repetition between 6 and 12-months after randomization, respectively (Table 3; Supplement 4, Figure S4.3.1a, available online). One study was excluded due to zero events in both arms. There was no evidence that interventions (overall or by intervention) were more or less effective than controls at reducing self-harm between 6 and 12 months or other time-periods using

FIGURE 2 Continued



IPD or IPD+AD; all CIs included the null effect and spanned mainly small (positive and negative) effects overall and small to large effects by intervention.

Overall, between-study heterogeneity was low at 6 to 12 months (IPD: $I^2 = 4.2\%$, $p = .405$; IPD+AD: $I^2 = 9\%$, $p = .352$) and 12 to 18 months (IPD: $I^2 = 20.1\%$, $p = .282$). There was no evidence of heterogeneity between groups of interventions; however, there was some evidence at the 10% level of between-study heterogeneity for 2 group therapy studies with contrasting effects at 6 to 12 months (IPD: $I^2 = 69.0\%$, $p = .072$; IPD+AD: $I^2 = 67.1\%$, $p = .081$) and 2 CBT studies at 12 to 18 months in adjusted IPD meta-analyses ($I^2 = 64.9\%$, $p = .092$).

General Psychopathology. Overall, 1,369 (71.9% eligible) participants (8 studies) and 1,564 (73.0% eligible) participants (10 studies) were included in IPD and IPD+AD meta-analyses at 12 months, respectively (Figure 3,

TABLE 4 Summary of 12-Month Meta-Analysis of Treatment Effect Estimates

	Adjusted IPD random-effects meta-analysis							Unadjusted IPD+AD random-effects meta-analysis						
	No. Studies	No. participants	Pooled effect	(95% CI)	I^2, p	τ^2	(95% CI)	No. Studies	No. participants	Pooled effect	(95% CI)	I^2, p	τ^2	(95% CI)
Repeat self-harm (randomization to 12 mo)			Odds ratio							Odds ratio				
CBT	7	483	1.45	(0.77, 2.73)	20.1%, 0.277	0	(0, 1.52)	7	483	1.40	(0.79, 2.47)	3.3%, 0.401	0.00	(0, 1.07)
DBT	1	28	1.31	(0.15, 11.26)	NA	NA		1	28	1.54	(0.16, 14.54)	NA	NA	
Family therapy	1	826	1.13	(0.81, 1.58)	NA	NA		1	826	1.13	(0.81, 1.58)	NA	NA	
Group therapy	2	437	1.28	(0.00, 6545.76)	72.2%, 0.058	0.67	(0, 117.02)	3	500	0.70	(0.02, 23.84)	76.2%, 0.015	1.49	(0, 35.28)
CAT/MBT	3	190	0.71	(0.10, 4.84)	25.2%, 0.263	0.08	(0, 11.27)	3	190	0.78	(0.16, 3.93)	8.3%, 0.336	0.00	(0, 8.27)
PST	3	339	0.94	(0.29, 3.03)	0.0%, 0.742	0	(0, 3.37)	3	339	0.97	(0.30, 3.14)	0.0%, 0.670	0.00	(0, 3.63)
Postcards/tokens	2	577	1.03	(0.02, 65.50)	0.0%, 0.810	0	(0, 16.94)	3	682	0.91	(0.25, 3.27)	0.0%, 0.623	0.00	(0, 3.45)
Brief intervention	1	69	0.47	(0.12, 1.89)	NA	NA		1	69	0.47	(0.11, 1.94)	NA	NA	
Overall	20	2,949	1.06	(0.86, 1.31)	1.1%, 0.443	0	(0, 16.94)	22	3,117	1.02	(0.82, 1.27)	12.1%, 0.299	0	(0, 0.21)
			Heterogeneity between groups: p = .779							Heterogeneity between groups: p = .759				
Time to SH			Hazard ratio							Hazard ratio				
CBT	1	50	1.85	(0.78, 4.42)	NA	NA		1	50	1.73	(0.73, 4.10)	NA	NA	
Family therapy	1	828	1.03	(0.83, 1.28)	NA	NA		1	828	1.04	(0.84, 1.28)	NA	NA	
Group therapy	2	439	1.14	(0.14, 9.55)	41.1%, 0.193	0.03	(0, 8.27)	2	439	1.17	(0.10, 14.01)	53.9%, 0.141	0.05	(0, 10.54)
PST	1	46	0.84	(0.27, 2.60)	NA	NA		1	46	0.92	(0.30, 2.86)	NA	NA	
Postcards/tokens	2	107	1.25	(0.00, 497.19)	0.0%, 0.594	0	(0, 26.93)	2	107	1.18	(0.00, 410.28)	0.0%, 0.537	0	(0, 28.41)
Brief intervention	1	69	0.68	(0.25, 1.86)	NA	NA		1	69	0.72	(0.27, 1.93)	NA	NA	
Overall	8	1,539	1.07	(0.90, 1.26)	0.0%, 0.693	0	(0, 0.15)	8	1,539	1.07	(0.90, 1.27)	0.0%, 0.706	0	(0, 0.15)
			Heterogeneity between groups: p = .722							Heterogeneity between groups: p = .813				
Pattern of self-harm (self-harm between 6 and 12 mo)			Odds ratio							Odds ratio				
CBT	4	216	0.90	(0.18, 4.67)	30.3%, 0.230	0.29	(0, 10.17)	4	216	0.92	(0.21, 4.11)	21.3%, 0.282	0.21	(0, 8.68)
DBT	1	24	1.69	(0.30, 9.52)	NA	NA		2	153	0.66	(0.01, 42.97)	0.0%, 0.333	0.00	(0, 47.00)
Family therapy	1	825	0.93	(0.59, 1.45)	NA	NA		1	825	0.93	(0.59, 1.46)	NA	NA	
Group therapy	2	436	1.28	(0, 463.54)	69.0%, 0.072	0.31	(0, 56.24)	2	436	1.25	(0, 319.24)	67.1%, 0.081	0.27	(0, 49.89)
CAT/MBT	3	188	0.81	(0.11, 5.99)	29.0%, 0.244	0.22	(0, 10.15)	3	188	0.85	(0.08, 8.72)	51.4%, 0.128	0.45	(0, 14.23)
PST	1	258	0.51	(0.19, 1.35)	NA	NA		1	258	0.49	(0.18, 1.33)	NA	NA	
Postcards/tokens	1	67	0.40	(0.05, 2.87)	NA	NA		1	67	0.50	(0.07, 3.72)	NA	NA	
Brief intervention	1	69	1.27	(0.24, 6.89)	NA	NA		1	69	1.40	(0.25, 7.81)	NA	NA	
Overall	14	2,083	0.93	(0.71, 1.23)	4.2%, 0.405	0	(0, 0.43)	15	2,212	0.90	(0.69, 1.16)	9.0%, 0.352	0	(0, 0.45)
			Heterogeneity between groups: p = .855							Heterogeneity between groups: p = .854				
General psychopathology			SMD							SMD				
CBT	3	187	−0.16	(−0.79, 0.48)	0.0%, 0.492	0	(0, 0.96)	3	187	−0.16	(−0.80, 0.48)	4.1%, 0.352	0	(0, 1.34)
DBT	0	0	—		—	—		1	133	−0.07	(−0.41, 0.27)	NA	NA	
Family therapy	1	465	−0.11	(−0.27, 0.04)	NA	NA		1	465	−0.19	(−0.37, −0.00)	NA	NA	
Group therapy	2	397	−0.35	(−3.47, 2.78)	67.0%, 0.082	0.09	(0, 16.18)	3	459	−0.26	(−0.86, 0.35)	33.4%, 0.223	0.03	(0, 1.16)
CAT/MBT	1	64	−0.20	(−0.65, 0.24)	NA	NA		1	64	−0.08	(−0.57, 0.41)	NA	NA	
PST	1	256	0.04	(−0.20, 0.27)	NA	NA		1	256	0.07	(−0.17, 0.32)	NA	NA	
Overall	8	1,369	−0.13	(−0.25, −0.01)	5.7%, 0.386	0	(0, 0.08)	10	1,564	−0.13	(−0.25, −0.02)	0.0%, 0.458	0	(0, 0.05)
			Heterogeneity between groups: p = .609							Heterogeneity between groups: p = .558				
Depression			SMD							SMD				
CBT	5	286	−0.08	(−0.41, 0.25)	0.0%, 0.830	0	(0, 0.20)	5	286	−0.05	(−0.38, 0.28)	0.0%, 0.847	0	(0, 0.19)
DBT	0	0	—	—	—		1	133	−0.14	(−0.48, 0.20)	NA	NA		
Family therapy	1	431	−0.04	(−0.22, 0.14)	NA	NA		1	431	−0.05	(−0.24, 0.14)	NA	NA	

(*continued*)

TABLE 4 Continued

	Adjusted IPD random-effects meta-analysis						Unadjusted IPD+AD random-effects meta-analysis					
	No. Studies	No. participants	Pooled effect	(95% CI)	I^2, p	T^2	(95% CI)	No. Studies	No. participants	Pooled effect	(95% CI)	I^2, p	T^2	(95% CI)
Group therapy	2	395	−0.19	(−2.33, 1.94)	44.6%, 0.179	0.03	(0, 8.50)	3	453	−0.13	(−0.74, 0.48)	34.2%, 0.219	0.02	(0, 1.24)
CAT/MBT	2	89	−0.40	(−3.28, 2.48)	0.0%, 0.735	0	(0, 16.16)	2	89	−0.34	(−3.05, 2.37)	0.0%, 0.688	0	(0, 10.63)
PST	2	280	0.05	(−1.42, 1.53)	0.0%, 0.807	0	(0, 4.17)	2	280	0.03	(−1.49, 1.54)	0.0%, 0.399	0	(0, 10.75)
Overall	12	1,481	−0.07	(−0.18, 0.04)	0.0%, 0.784	0	(0, 0.04)	14	1,672	−0.07	(−0.17, 0.04)	0.0%, 0.856	0	(0, 0.03)
	Heterogeneity between groups: p = .432							Heterogeneity between groups: p = .746						
	SMD							SMD						
Suicide ideation														
CBT	3	166	−0.18	(−1.10, 0.73)	27.2%, 0.253	0.05	(0, 2.35)	3	166	−0.20	(−1.08, 0.67)	25.0%, 0.264	0.04	(0, 2.14)
DBT	1	23	−0.15	(−1.01, 0.70)	NA	NA		2	153	−0.05	(−2.11, 2.01)	0.0%, 0.516	0.00	(0, 7.0)
Family therapy	1	459	−0.15	(−0.33, 0.02)	NA	NA		1	459	−0.14	(−0.33, 0.04)	NA	NA	
Group therapy	2	395	−0.07	(−1.24, 1.10)	0.0%, 0.376	0	(0, 3.86)	3	452	−0.06	(−0.47, 0.34)	0.0%, 0.608	0	(0,0.47)
PST	2	280	−0.01	(−1.48, 1.46)	0.0%, 0.452	0	(0, 8.41)	2	280	0.02	(−1.50, 1.53)	0.0%, 0.505	0	(0, 8.21)
Overall	9	1,323	−0.09	(−0.21, 0.03)	0.0%, 0.734	0	(0, 0.05)	11	1,510	−0.08	(−0.20, 0.03)	0.0%, 0.823	0	(0, 0.04)
	Heterogeneity between groups: p = .868							Heterogeneity between groups: p = .822						

Note: Full results are in Supplement 6, available online. AD = aggregate data; CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; IPD = individual participant data; NA = not applicable; Postcards/tokens = postcards, tokens, documents; PST = problem solving, psychoeducation, support.

Table 2). There was good evidence of a small positive effect, indicating that interventions overall were more effective than control at reducing general psychopathology using IPD (SMD −0.13 [95% CI −0.25, −0.01], 8 studies, 1,369 participants) and IPD+AD (SMD −0.13 [95% CI −0.25, −0.02], 10 studies, 1,564 participants). Between-study heterogeneity was low (IPD: $I^2 = 5.7\%$, $p = .386$; IPD+AD: $I^2 = 0\%$, $p = .458$), and there was no evidence of heterogeneity between studies or groups of interventions. Effects were consistently positive, but not statistically significant, at other time points.

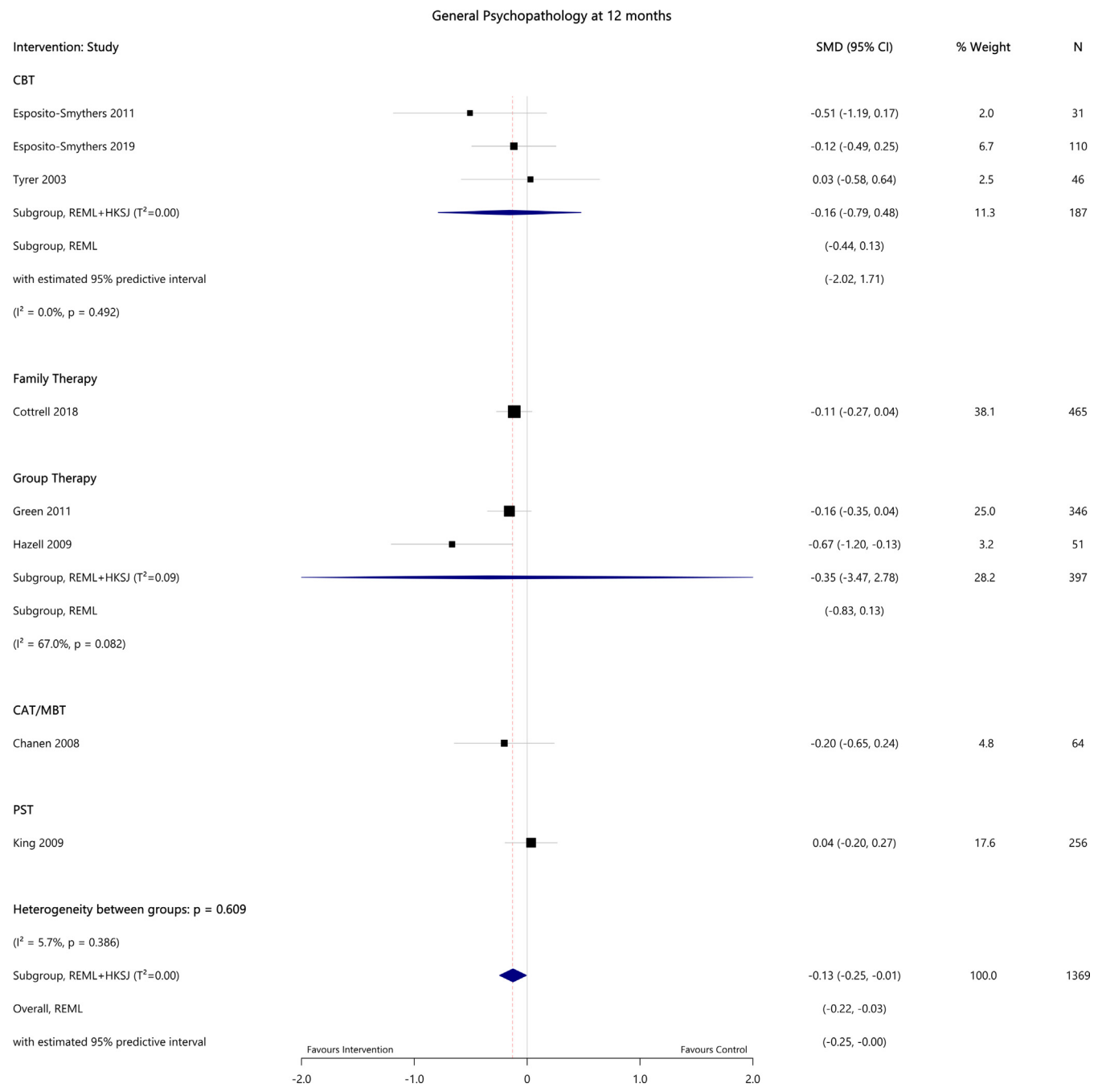
There was insufficient evidence to detect a statistically significant reduction compared with control at 12 months using IPD or IPD+AD for specific interventions; CIs were wide, spanning small to large positive and negative effects. There was evidence of a statistically significant reduction in general psychopathology for specific interventions compared with control from IPD when only single studies were available for (Supplement 4 and Supplement 6, available online): PST at 3 and 6 months; DBT at 6 months, but not when including 2 additional studies with AD; and CBT at 18 months.

There was again some evidence of between-study heterogeneity for 2 group therapy studies in IPD ($I^2 = 67.0\%$, $p = .082$), but not IPD+AD, analyses at 12 months. There was further statistical evidence of between-study heterogeneity in the overall treatment effect in IPD, but not IPD+AD, meta-analyses at 3 months due to the large treatment effect observed for 1 study of PST in adjusted analysis and at 6 months due to larger treatment effect estimates observed for 1 DBT and 1 PST study.

Depression. Overall, 1,481 (67.9% eligible) participants (12 studies) and 1,672 (69.1% eligible) participants (14 studies) were included in IPD and IPD+AD meta-analyses at 12 months, respectively (Table 2; Supplement 4, Figure S4.6.3, available online). There was no evidence that therapeutic interventions (overall or by intervention) were more or less effective than controls at reducing depression using IPD or IPD+AD at any time point; all CIs included the null effect and spanned mainly small (positive and negative) effects overall and small to large effects by intervention.

There was no evidence of heterogeneity between groups of interventions at any time point. There was statistical evidence of between-study heterogeneity in the overall treatment effect at 18 months in IPD and IPD+AD meta-analyses, driven by conflicting effect estimates between 2 studies of CBT. There was also statistical evidence of heterogeneity between 2 studies of family therapy at 3 months and some evidence at 6 months in IPD meta-analysis only and between 3 studies of PST at 6 months in adjusted IPD meta-analysis only.

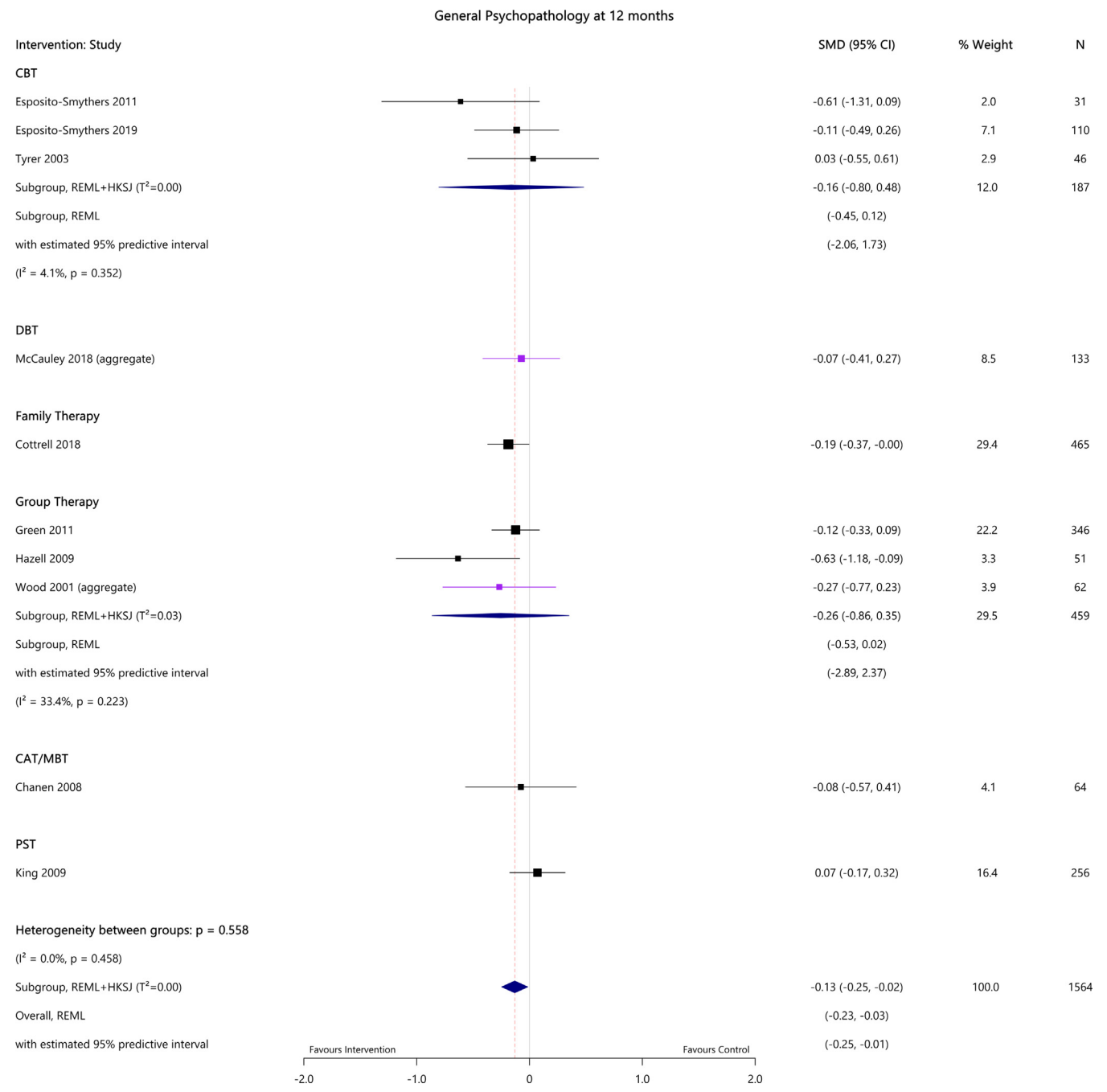
FIGURE 3 Forest Plots of the Effect of Intervention vs Control on General Psychopathology (GP) at 12 Months



Note: *References to included studies can be found in Table 1, references 34-72. The first panel depicts adjusted individual participant data (IPD) meta-analysis. The second panel depicts unadjusted IPD and aggregate data (AD) meta-analysis. Purple color coding highlights studies where estimates are from AD. CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; HKSJ = Hartung-Knapp-Sidik-Jonkmann; PST = problem solving, psychoeducation, support; REML = restricted maximum likelihood. Please note color figures are available online.*

Suicidal Ideation. Overall, 1,323 (70.0% eligible) participants (9 studies) and 1,510 (72.2% eligible) participants (11 studies) were included in IPD and IPD+AD meta-analyses at 12 months, respectively (Table 2; Supplement 4, Figure S4.7.3, available online). There was no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control at reducing suicidal ideation using IPD or

FIGURE 3 Continued



IPD+AD and no evidence of between-study heterogeneity or heterogeneity between groups of interventions at 3, 12, or 18 months.

Evidence of a small positive effect of intervention compared with control was observed at 6 months (Supplement 4 and Figure S4.7.3, available online) in IPD+AD meta-analysis (SMD −0.17 [95% CI −0.32, −0.02], 15 studies, 1,418 participants); however, this effect was not supported by IPD meta-analysis with fewer studies (2 DBT, 1 family therapy). The positive overall effect observed was driven largely by small to moderate effects for DBT (SMD −0.43 [95% CI −0.90, 0.03], 4 studies, 258 participants), CBT (SMD −0.24 [95% CI −0.90, 0.42], 3 studies, 170 participants) and family therapy (SMD −0.15 [95% CI −0.95, 0.65], 3 studies, 261 participants).

There was evidence at the 10% level of heterogeneity between the 2 family therapy studies at 6 months in IPD meta-analysis, but not IPD+AD meta-analysis including an additional study. There was also evidence of heterogeneity between groups of interventions at 6 months in IPD+AD meta-analysis ($p = .094$) driven by the range of effects observed for DBT, CBT, and family therapy and null effects found for group therapy and PST.

Assessment of Publication Bias and Small Study Effect. Funnel plots showed no evidence of small study effects or publication bias, with a few exceptions. Outlying studies with positive treatment effects and a lack of symmetry were observed for IPD+AD meta-analysis of general psychopathology at 6 and 12 months. Pooled treatment effect estimates from 1-stage fixed-effects IPD meta-analysis were comparable to random-effects IPD meta-analysis at 12 months but extenuated the treatment effect at 6 months.

Lack of symmetry was observed for IPD+AD meta-analysis of depression at 6 months (Egger's test $p = .024$) and suicidal ideation at 3 and 6 months (Egger's test $p = .063$ and $p = .021$, respectively); however, this was less pronounced for adjusted IPD meta-analysis, and 1-stage fixed-effects and 2-stage random-effects IPD meta-analysis were comparable.

Sensitivity Analysis. Two-stage IPD meta-analysis with multiple imputation gave similar results overall and by intervention compared with primary complete case analysis except for 3-month depression outcomes for family therapy interventions, where there was a reduction in the magnitude of the pooled treatment effect estimate and no longer significant between-study heterogeneity. One-stage random-effects IPD meta-analysis gave similar pooled treatment effect estimates compared with the primary 2-stage approach, with generally wider CIs both overall and by intervention.

One-stage fixed-effects IPD meta-analysis resulted in pooled treatment effect estimates that were generally comparable or closer to the null with tighter CIs compared with estimates obtained in primary random-effects IPD meta-analyses. Nevertheless, there were few changes to conclusions except for general psychopathology, where smaller CIs for fixed-effects estimates gave significant evidence that interventions overall and group therapy interventions were more effective than control at 6 months, as were group therapy interventions at 12 months. Additional sensitivity analysis of 2-stage IPD+AD meta-analysis on pattern of self-harm outcomes to explore the impact of zero events in 1 arm found no change to conclusions.

Additional Outcomes

Quality of life was available for 670 (59.3% eligible) participants (5 studies) with IPD and no participants with AD at 12 months. There was no evidence that interventions were more or less effective than controls in individual studies; estimated effects were small to moderate and positive in all but 1 study. However, CIs all included the null effect and spanned positive and negative small to large effects.

Adolescent deaths were reported for 11 eligible participants in 7 studies (6 IPD, 1 AD; 7 intervention, 4 control) and for 2 participants (1 control, 1 unknown) in 2 partially eligible studies in which eligibility could not be determined. No eligible participants died in 10 studies, and no deaths were reported in the remaining 20 studies.

Participant Moderators

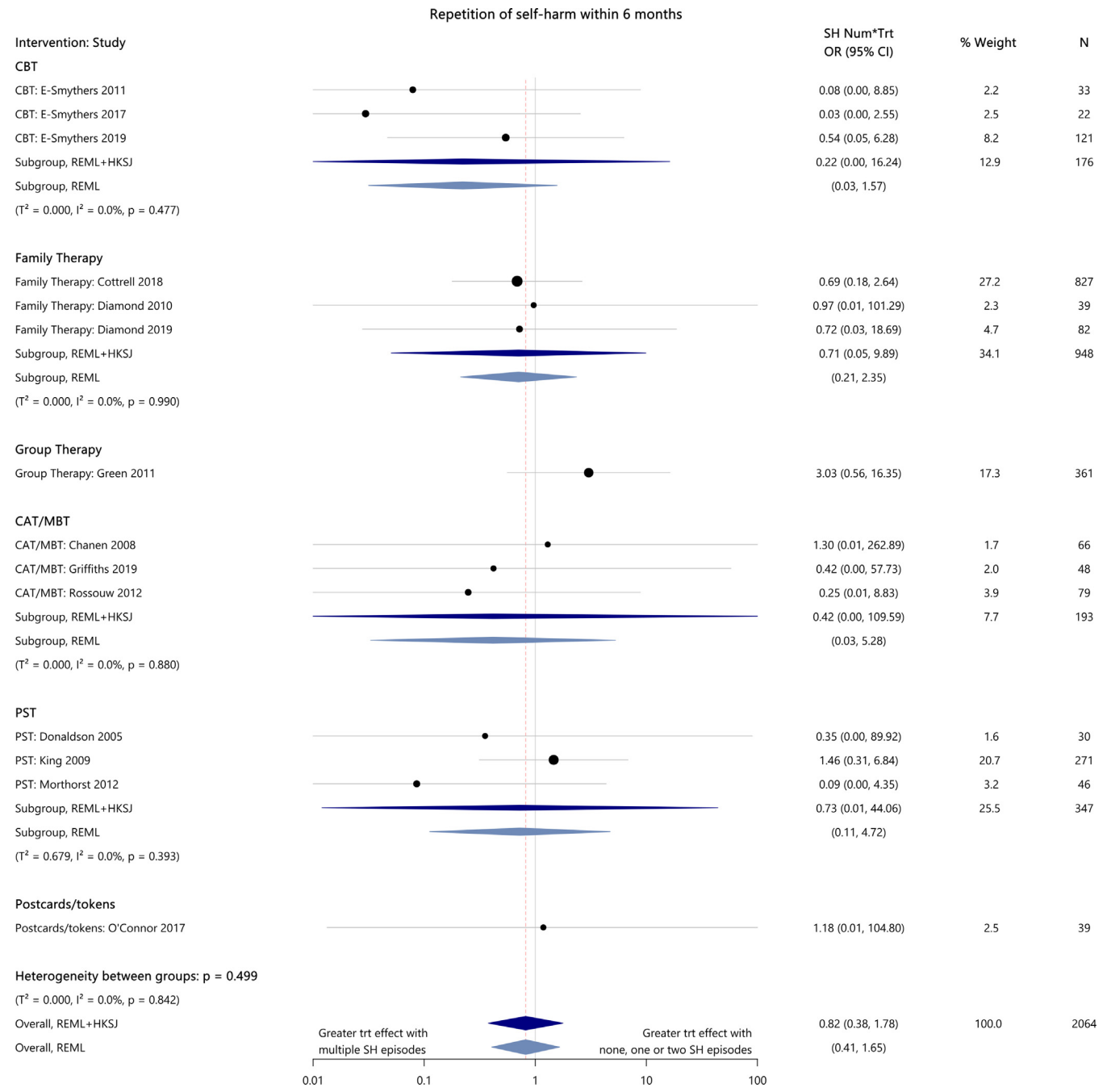
Our analysis focused on the 6- and 12-month time points as they encompassed all studies with available outcomes (further details are in Supplement 3 and Supplement 5, available online). We found no evidence of moderating effects on primary or secondary outcomes, overall or in specific groups of interventions, according to key moderators of participants' age, gender, depression, method of self-harm, or borderline personality disorder diagnosis, or on repeated self-harm outcomes, according to additional moderators of anxiety, family dysfunction, ethnicity, psychotropic medication, or suicidal ideation.

There was evidence of an improved treatment effect in participants with multiple previous self-harm episodes compared with participants with fewer ($\leq$2) or no prior self-harm episodes on repeat self-harm episodes within 6 to 12 months (OR 0.33 [95% CI 0.12, 0.94], 9 studies, 1,771 participants) (Figure 4). This interaction should be considered alongside the overall treatment effect, which showed a nonsignificant 7% reduction in the likelihood of repeat self-harm in intervention vs control (OR 0.93 [95% CI 0.71, 1.23], 14 studies) (Figure 2). A more favorable, but not statistically significant, treatment effect was similarly indicated in participants with multiple previous self-harm episodes on primary repeat self-harm outcomes at 6 and 12 months, general psychopathology, and suicidal ideation outcomes and on 12-month, but not 6-month, depression outcomes. There was no evidence of variability between studies, heterogeneity among different groups of interventions, or variability within groups of interventions.

Assessment of Publication Bias and Small Study Effect of Participant Moderators

Funnel plots for all moderators and outcomes and regression-based Egger's tests (Figures S4.1.3–S4.13.2,

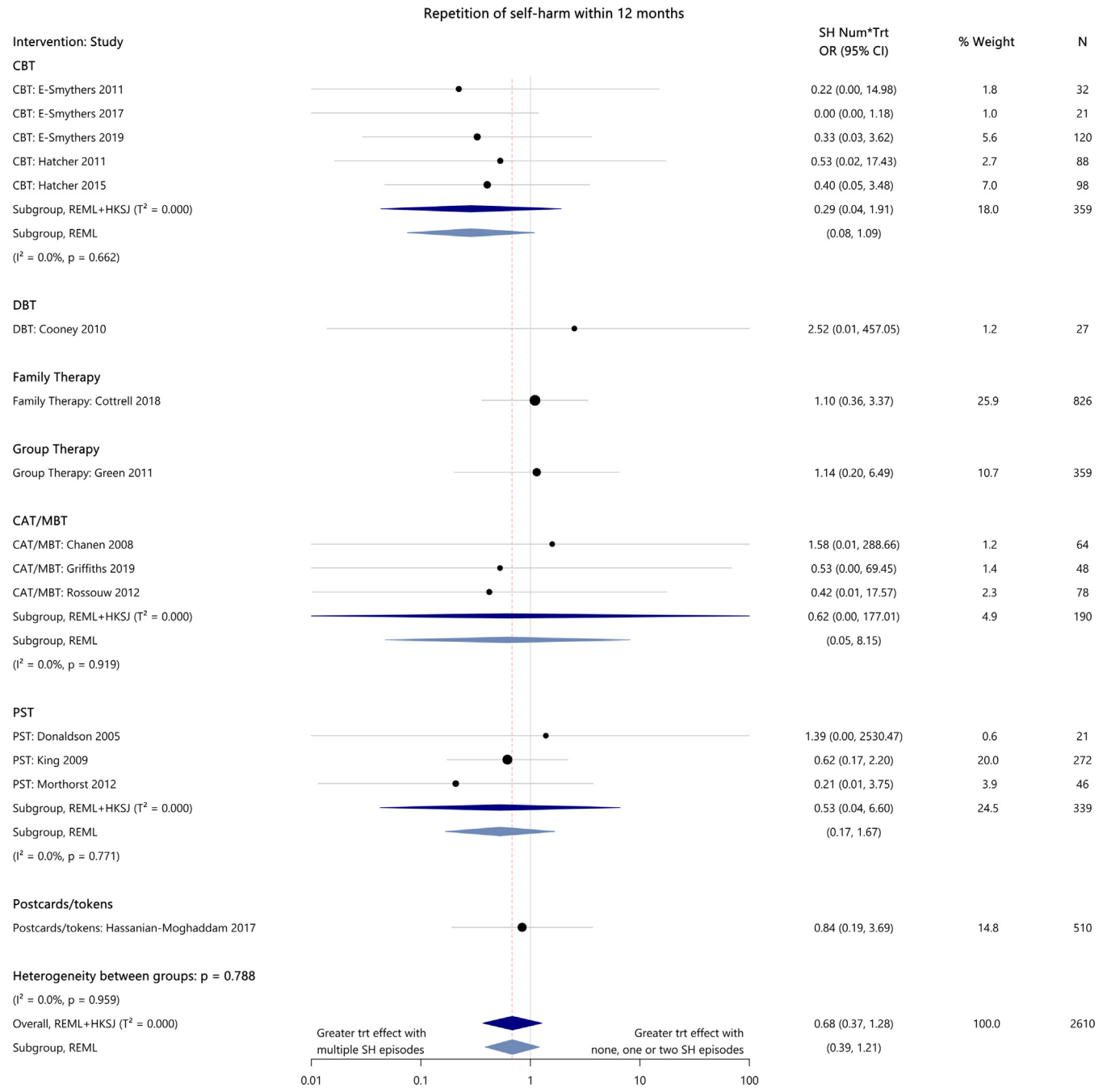
FIGURE 4 Forest Plots of the Differential Effects for Intervention vs Control According to Participants' Number of Self-Harm (SH) Episodes



Note: References to included studies can be found in Table 1, references 34-72. The first panel depicts repetition of SH within 6 months. The second panel depicts repetition of SH within 12 months. The third panel depicts repetition of SH between 6 and 12 months. The fourth panel depicts general psychopathology, the fifth panel depicts depression, and the sixth panel depicts suicidal ideation. The x-axis presents the OR. See Supplement 5, available online, for associated subgroup effects. CAT/MBT = cognitive analytic therapy and mentalization-based therapy; CBT = cognitive-behavioral therapy; DBT = dialectical behavior therapy; HKSJ = Hartung-Knapp-Sidik-Jonkmann; Postcards/tokens = postcards, tokens, documents; PST = problem solving, psychoeducation, support; REML = restricted maximum likelihood; trt = treatment. Please note color figures are available online.

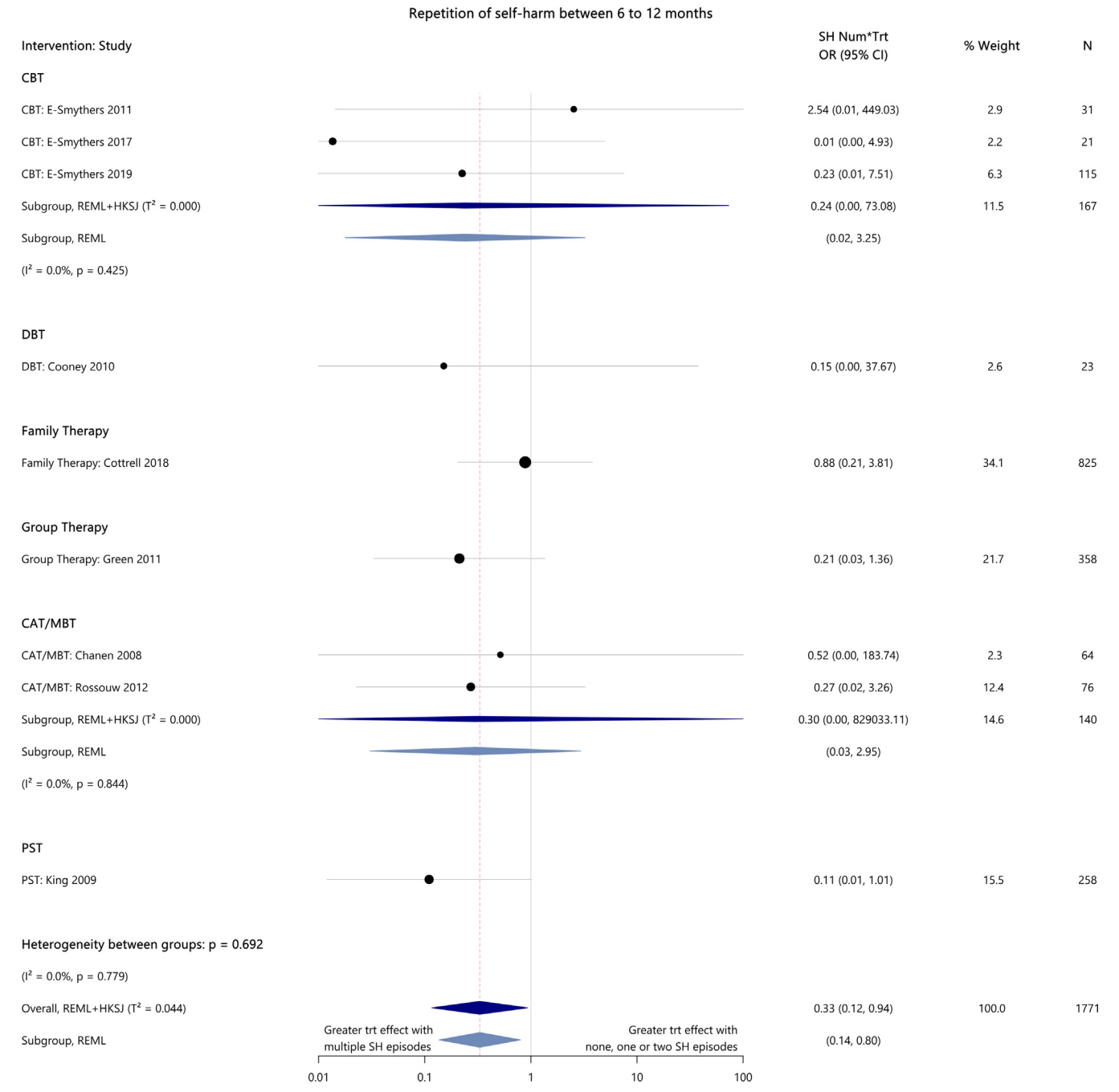
Table S2, available online) generally indicated no evidence of small study effects or publication bias. The notable exception was the moderating effect of the level of depression on the primary outcome at 12 months, where some evidence of publication bias was observed ($p = .0638$).

FIGURE 4 Continued



Sensitivity Analysis of Participant Moderators. In sensitivity analysis in which CIs for combined treatment effects were calculated without the Hartung-Knapp-Sidik-Jonkmann[29] adjustment (indicated by CI*), results appeared more precise due to the exclusion of uncertainty in estimated between-study heterogeneity. This change in methodology identified PST as more effective for older participants on 6-month repetition of self-harm (OR 0.56 [95% CI* 0.26, 0.90], 4 studies, 400 participants) (Figure S5.1.1, available online) and suicidal ideation (SMD −0.19 [95% CI* −0.36, −0.03], 3 studies, 319 participants) (Figure S5.1.2, available online) outcomes and CBT as more effective for male participants on depression outcomes at 6 months (SMD −0.70 [95% CI* −1.39, −0.02], 3 studies, 190 participants) (Figure S5.2.2, available online) and 12 months (SMD −0.69 [95% CI* −1.39, −0.0], 4 studies, 216 participants) (Figure S5.2.2, available online). These effects were primarily influenced by a more pronounced

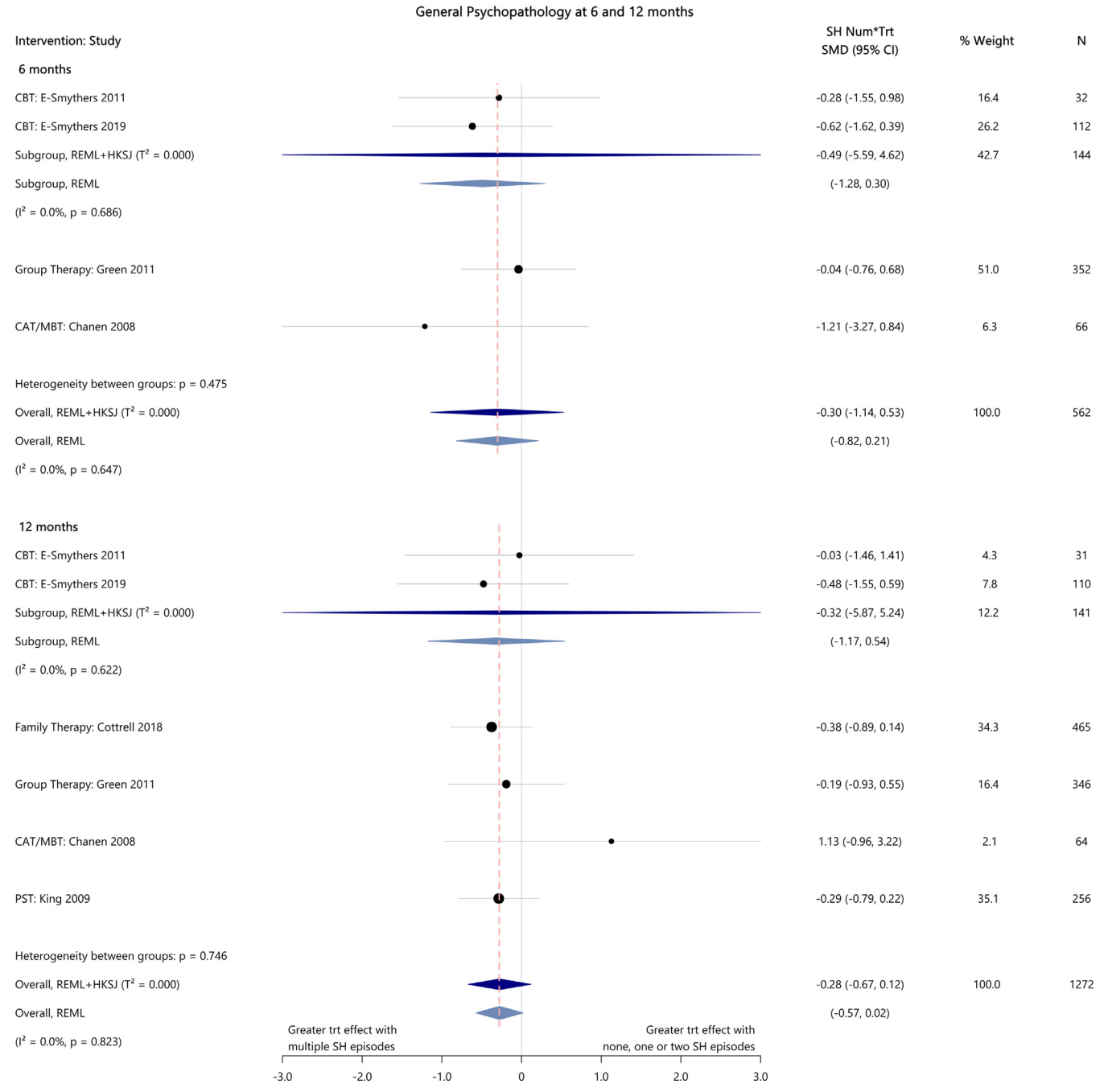
FIGURE 4 Continued



treatment effect in older participants in the King *et al.*[59] study and in male participants in the Esposito-Smythers *et al.*[47] study. However, there was no evidence of variability between studies.

Heterogeneity of Participant Moderators. Heterogeneity, both between studies and by and within studies of specific interventions, was observed across a range of examined moderators and outcomes where no evidence of a participant-level moderating effect was observed. These included moderators of age, self-harm method, borderline personality disorder, depression, family dysfunction, and particularly between study variability in 2 group therapy studies and varying CBT and PST studies.

FIGURE 4 Continued



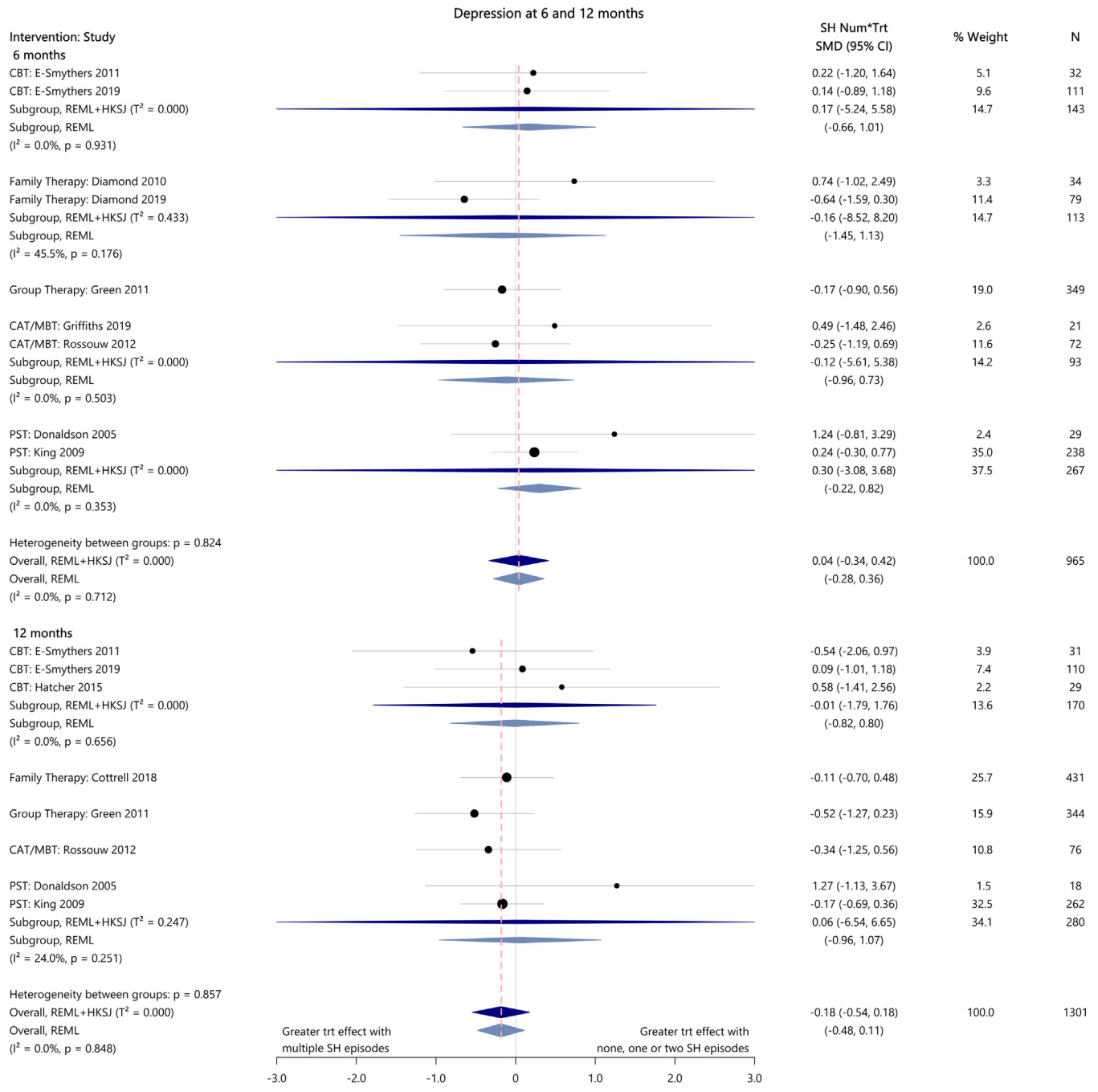
DISCUSSION

Summary of Evidence

We identified 39 studies that met our inclusion criteria. Our IPD analysis set comprised 26 studies with 3,448 eligible participants, and additional AD from 7 studies with 698 participants were included in IPD+AD meta-analysis. For our primary outcome, repetition of self-harm, only 6 of 39 studies were rated as low risk of bias, and 8 of 39 studies were rated as high risk.

Primary Outcome. There was no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control for reducing repeat self-harm between randomization and 3, 6, 12, 18, 24, or >24

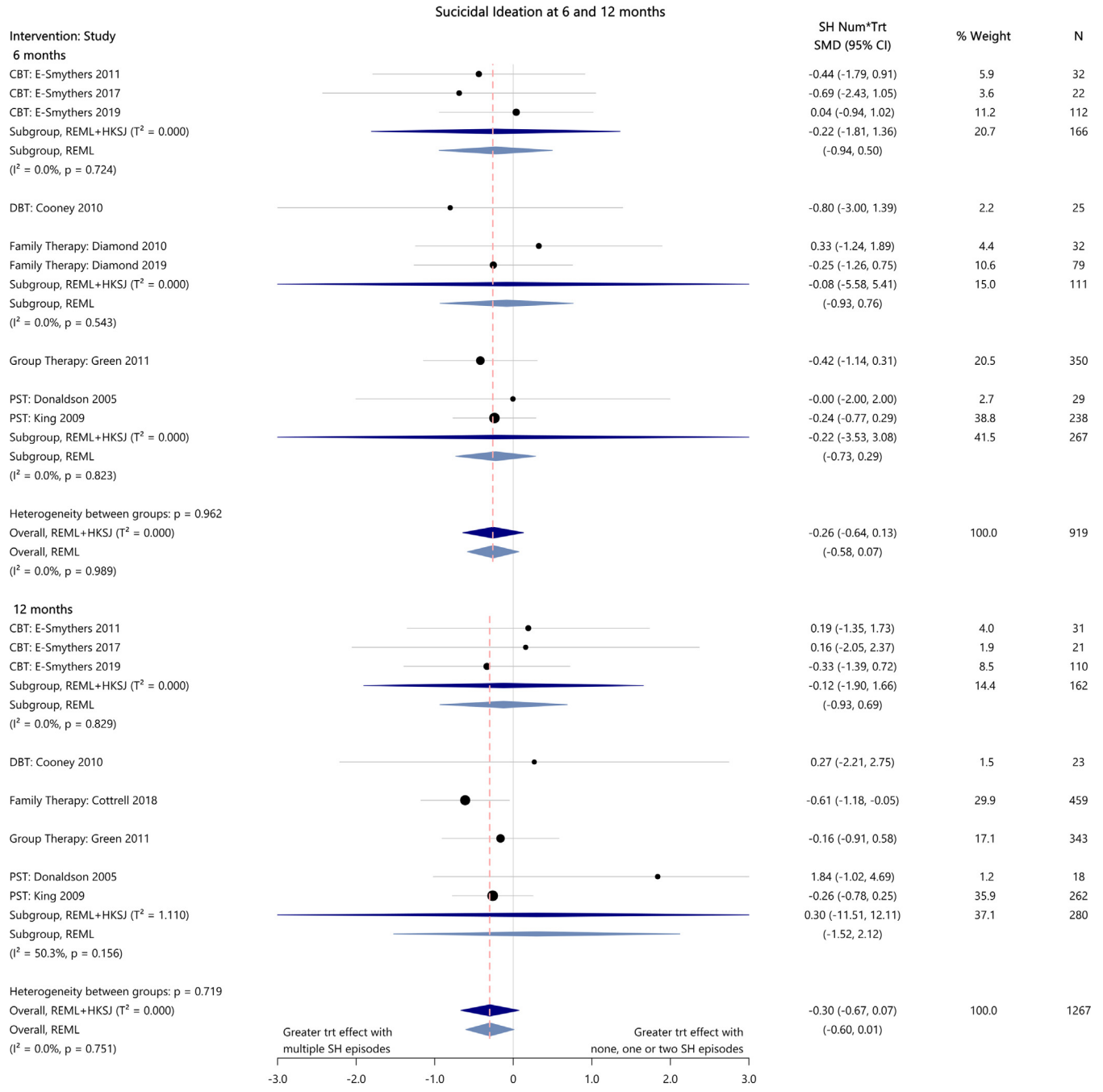
FIGURE 4 Continued



months. There were high levels of within-study variability in outcomes and generally low between-study heterogeneity in treatment effects, with the exception of a few studies of CAT/MBT at 3 months, group therapy at 12 months, and CBT at 18 months. We found no evidence for candidate moderator study or treatment effects, small study effects or publication bias, and sensitivity analyses led to no changes to our conclusions.

Secondary Outcomes. We found no evidence that any therapeutic intervention (overall or by intervention) was more or less effective than control on time to repetition of self-harm, pattern of self-harm repetition (within 6-month periods after randomization), or depression at any time point. There was good evidence that interventions overall had a small positive effect on general psychopathology at 12 months in IPD and IPD+AD meta-analysis; however, there

FIGURE 4 Continued



was insufficient evidence for specific interventions (with only 1-3 studies available per intervention). There was no further evidence for any therapeutic intervention overall at other time points. There was some limited evidence from single studies in support of CBT,[45] DBT,[67,68] and PST[64] at certain time points using IPD, but this was not supported for DBT when including additional AD.

There was good evidence that interventions overall had a small positive effect on suicidal ideation at 6 months in IPD+AD meta-analysis.[39,60,61,67,68] There was insufficient evidence for specific interventions (with only 2-4 studies available per intervention); however, the overall treatment effect was subject to heterogeneity between groups of interventions driven by the moderate and small positive

(nonsignificant) effects observed for DBT and CBT compared with other interventions. This finding was not detected at other time points or in IPD meta-analysis in which IPD for some DBT studies were not available.

Participant Moderators. There was a notable improvement in treatment effect for participants with multiple previous self-harm episodes compared with participants with fewer episodes on repetition of self-harm 6 to 12 months after randomization, accompanied by a consistent trend across other outcomes. There was more limited evidence for potential differential treatment effects based on participants' age and gender in PST and CBT respectively, as indicated by CIs not adjusted for uncertainty in variance estimates.

The strengths of this study are that an IPD meta-analysis provides more robust estimates of the effects of therapeutic interventions for self-harm compared with conventional meta-analyses that rely on AD and reported analyses.[15] The IPD approach enables a consistent and comprehensive analysis across a wide range of studies, outcomes, and moderators, significantly enhancing the power to detect interaction effects. This capability surpasses what can be achieved through single trials or AD meta-analysis. This IPD meta-analysis represents a pioneering effort in this specific population. Before this, no similar IPD meta-analysis had been conducted, marking this study as the first of its kind to explore the critical clinical problem of adolescent self-harm.

Rigorous inclusion criteria and inclusion of trial registrations in the search allowed us to minimize selection and publication bias. All records were screened independently by 2 authors, with a third adjudicating if an agreement could not be reached. Participants in eligible studies must have self-harmed leading to contact with services before randomization, thus excluding studies using nonclinical samples and making our participants generally more troubled and in need of services. We had a broad geographical spread of studies. The IPD approach allowed us to include studies where only a part of the sample was eligible. We were able to identify 21 additional studies (approximately 2,217 participants) and obtain IPD for 1,783 participants from 16 of these studies, providing more studies and participants for whom we were able to obtain IPD than from studies in which the full sample were eligible. The most recent Cochrane review[10] included only 17 trials with a total of 2,280 participants. The inclusion of substantially more studies and participants than in previous reviews has narrowed CIs, increased precision, and given more confidence in our findings. The use of subsamples from studies not included in other reviews also enabled us to include and report on interventions, such as postcards, that have either not been included or included only in small numbers in other meta-analyses.

Finally, an additional strength came from inviting the original study authors who shared data to join our study collaborative group. This collaboration allowed for their contributions to the development of the analysis plan and the interpretation of results, thus enhancing the trustworthiness of findings.

A limitation of this study is that the eligible RCTs we identified were conducted by various groups worldwide over several decades, differing in therapeutic orientation, intensity and duration of intervention, controls, aims, outcomes, and targeted subsets of adolescents. Given the seriousness of the clinical problem, it is surprising how few good quality studies we identified. The wide variety of interventions within the eligible studies meant that for any single intervention, there were few good quality studies, and for some intervention types, very few, with some subgroup analyses based on only 1 study. Replication was lacking. In the single instance of study replication, the replication by Hazell *et al.*[54] of a study by Wood *et al.*[71] resulted in the earlier findings being contradicted.

A significant limitation was missing IPD, with some authors being unable to share data despite our willingness to receive reduced datasets addressing concerns about participant identification. In some cases, data had been lost or destroyed. Whereas IPD+AD meta-analysis was able to incorporate AD from studies lacking IPD, this was not possible for studies in which only a subset of participants was eligible and published AD pertained to the full sample or studies in which insufficient AD were reported and the full sample was eligible.

We were unable to obtain IPD for 2 important studies (both rated as some concerns of risk of bias) that are often cited in systematic reviews and meta-analyses as showing evidence for effectiveness of DBT.[60,73] Accordingly, our IPD meta-analysis includes only 2 small underpowered studies of DBT.[39,67,68] This is a clear limitation; however, we were able to incorporate AD from the published results of these 2 studies in our IPD+AD meta-analysis. This did not lead to any change in our conclusions.

A major challenge is the variability in the definitions of outcomes, timing, methods, and measures used for data collection across studies of self-harm interventions, which potentially increases between-study heterogeneity and limits the ability to meaningfully pool studies and interpret pooled treatment effects. Regarding timing, we defined multiple follow-up time points to pool treatment effects over consistent periods of time across studies. Whereas this ensured consistency in timing, it also increased the number of separate meta-analyses each containing fewer studies than

had we selected a single but variable postintervention time point for each study. Methods of data collection also varied from self-report, parent-report, clinical interview or rating, and medical record review. At least 8 different measures were used to collect self-harm, general psychopathology, and depression outcomes.

Studies also used variable age ranges, perhaps reflecting different patterns of care in the locations where studies were conducted. Our choice of 11 to 18 years of age (up to the 19th birthday) will have implications for interpretation in places where different age cut points are used by local services. Our choice was largely determined by the cut points used in other large reviews.[8-10]

The paucity of data across common outcomes and follow-up durations significantly constrained our exploration of potential participant moderators. Apart from age and gender, other baseline characteristics such as ethnicity, family dysfunction, psychotropic medication use, LGBTQ status, autistic spectrum disorder, history of abuse, eating disorders, intellectual disability, children in out-of-home placement, and physical health problems were inconsistently collected. There was also variability in the measures and methods used for collecting data on moderators and outcomes. Standardization of effects within each study and by time point was employed where possible to address this issue. While the IPD method allowed us to include subsets of participants from larger studies, these larger studies often focused more on adults, making them less likely to include characteristics specific to children and adolescents.

Our choice of a binary primary outcome of any repetition of self-harm could be seen as a limitation, but was chosen considering the serious difficulties in accuracy and consistency of alternative measurements, such as the number/frequency of self-harm episodes across studies, particularly for participants who engage in self-harm repeatedly. However, relevant outcomes varied considerably across studies, as well as the measures used to collect outcomes, and included NSSI, hospital attendance for self-harm/self-poisoning, suicide attempt, parasuicidal behavior, and unspecified self-report. Therefore, our primary outcome described whether young people had self-harmed or not at 12 months, not a reduction in the number of self-harm attempts, and our conclusions need to be understood in this light. Evidence from individuals with lived experience of NSSI suggest that recovery needs to be understood in more complex ways than just cessation or reduced frequency of self-harming behavior.[74]

Finally, it should be noted that when fewer than 10 trials are included in a meta-analysis, or trials are small, or the outcome is rare, no currently available method can reliably estimate the heterogeneity.[28] More sophisticated analysis approaches were considered to account for some of the further data complexities, but it was thought that although none would alter the conclusions materially, they would add to the complexity of conducting and reporting the analyses. These are left for future research.

We had hoped that using IPD methods would provide more accurate information about effective interventions and identify subgroups of young people who might benefit from specific types of intervention. However, we were unable to fully achieve these aims. Although IPD allowed us to include substantially more studies and participants, we still pooled a relatively small number of studies once different interventions, end points and follow-up times were considered. Whereas IPD meta-analysis remains a potentially powerful tool, its effectiveness depends on the quantity and quality of the studies it draws upon.

Nevertheless, we argue that this robust reinforcement of the broad message from other reviews is clinically important. It serves as a counterweight to some assessments of the long-term effectiveness of psychological therapies for treating self-harm in adolescents, which are often based on relatively small (underpowered) studies. We did not reach the same conclusion as Kothgassner *et al.*[11] that, overall, any intervention is more effective than active controls. Our findings also suggest caution regarding the effectiveness of DBT. The most recent NICE guideline recommended consideration of DBT-A for children and young people, but could not make a strong recommendation due to limited evidence on repeat self-harm by 12-month follow-up. This recommendation was based on a recent Cochrane review,[10] which found positive effects of DBT-A on repetition of self-harm after intervention as well as improved depression, hopelessness, and suicidal ideation outcomes in the short term. These short-term findings align with our 6-month time point and were observed immediately after the intensive treatment ended. However, these effects were not present at our 12-month analysis. Therefore, despite the public health importance of self-harm, its many adverse outcomes, and a rigorous IPD meta-analysis design, we cannot recommend a specific, safe intervention for the prevention of self-harm repetition among young people who present with self-harm. Why might this be?[75]

Ethical concerns have meant that except for very low intensity postcard-type interventions, all the studies we examined looked at specific intervention types compared with a control treatment, not a no treatment control. Control treatments varied widely from TAU to active manualized specific treatments, including antidepressant pharmacotherapy, family-enhanced nondirective supportive therapy, supportive relationship treatment, hospitalization,

and individual and group supportive therapy. Therefore, overlap of treatment components is likely not just between different interventions but between intervention and control treatments. Well-trained clinicians are likely to be well versed in the existing evidence base, and so some or many TAU control interventions may also be effective. Thus, both arms in some RCTs may have received comprehensive care, thereby reducing treatment effect sizes. It is possible that practitioners delivering control treatments used some of the same techniques specified in intervention arms, but even if this did not occur, staff seeing control arm participants were able to conduct assessments and tailor their interventions to individual needs, perhaps in a more flexible way than in the manualized intervention arm where only the target intervention could be delivered.

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

Finally, it is important to stress that, in line with the conclusions of the most recent Cochrane review,[10] we found no evidence that interventions were more or less effective than control treatments. We did not find that treatments were ineffective. Clinicians should not interpret these findings as meaning that interventions do not work, but rather that we do not yet know which interventions are effective for which young people. It is important to emphasize that young people who self-harm are at elevated risk for many adverse outcomes and should undoubtedly receive help and support. Our findings indicate that young people who have engaged in recurrent self-harm (defined here as more than 2 previous episodes) might respond more positively to treatment. Given their higher risk, it is imperative that they are thoroughly assessed and offered an intervention deemed most appropriate by a trained and qualified clinician.

Future recommendations include the need for innovative ideas to optimize standard care and develop alternative interventions. These should be more deeply grounded in theoretical considerations or mechanisms that drive self-harm. Collaborative research programmes are essential to rapidly execute large-scale, well-designed studies and to establish core outcome sets of trials of self-harm interventions. Given how difficult it is to alter the developmental trajectories of individuals who self-harm, it is also crucial to explore prevention strategies.

Future evaluations of therapeutic interventions for adolescents following self-harm should employ novel and efficient clinical trial designs to optimize existing therapeutic approaches or TAU, for example, through a SMART design,[76] and ensure larger comparative head-to-head comparisons of interventions and tailor intervention strategies, such as through platform[77] or factorial[78] trial designs that focus on optimizing fixed or adaptive interventions. These approaches are better suited to address multiple research questions and determine the most effective interventions for different individuals, while simultaneously ensuring consistency in research methods.

It seems unlikely that future IPD meta-analyses in this area will be fruitful until we have more well-designed and well-conducted studies that use agreed outcome measures. Future research to develop and agree on core outcome sets for self-harm trials is vital. More detailed reporting of control arm interventions would increase the homogeneity of outcome reporting, allowing future studies to be pooled more efficiently and inclusively.[75] Establishing a clear and agreed-upon definition of the primary outcome with standardized follow-up times is crucial, given the complex nature of self-harm and its related outcomes. There should be consensus on the moderators to be included in future studies. It is important to consider participant-level treatment effect moderators during trial design to ensure that the study is tailored to detect important differences and trends. Many important moderators are currently inconsistently collected. Ensuring that these are consistently included in future research will greatly enhance the quality and applicability of the findings. Additionally, interventions delivered in control groups should be better measured and accounted for in analyses.

Research funders play a crucial role in developing a comprehensive plan for future trials and data collection. They can facilitate this by commissioning the organization of international conferences or a series of meetings for the scientific and service user communities and subsequently requiring changes in funded projects. Funders should also ensure that future trials include appropriate consent to allow data sharing for meta-analysis.

CRediT authorship contribution statement

Alex Wright-Hughes: Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Amanda J. Farrin:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition,

Conceptualization. **Peter Fonagy:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Dennis Ougrin:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Daniel Stahl:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Judy Wright:** Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Funding acquisition, Conceptualization. **Donna Irving:** Writing – review & editing, Writing – original draft, Project administration, Investigation. **Faraz Mughal:** Writing – review & editing, Investigation. **Alex Truscott:** Writing – review & editing, Investigation. **Emma Diggins:** Writing – review & editing, Investigation. **Andrew Chanen:** Writing – review & editing, Data curation. **Emily Cooney:** Writing – review & editing, Data curation. **Greg Carter:** Writing – review & editing, Data curation. **Kerrie Clover:** Writing – review & editing, Data curation. **Mark Dadds:** Writing – review & editing, Data curation. **Guy Diamond:** Writing – review & editing, Data curation. **Christianne Esposito-Smythers:** Writing – review & editing, Data curation. **Jonathan Green:** Writing – review & editing, Data curation. **Helen Griffiths:** Writing – review & editing, Data curation. **Hossein Hassanian-Moghaddam:** Writing – review & editing, Data curation. **Simon Hatcher:** Writing – review & editing, Data curation. **Philip Hazell:** Writing – review & editing, Data curation. **Nusrat Husain:** Writing – review & editing, Data curation. **Michael Kaess:** Writing – review & editing, Data curation. **Cheryl King:** Writing – review & editing, Data curation. **Britt Morthorst:** Writing – review & editing, Data curation. **Rory C. O'Connor:** Writing – review & editing, Data curation. **Pilar Santamarina-Perez:** Writing – review & editing, Data curation. **Peter Tyrer:** Writing – review & editing, Data curation. **Rebecca Walwyn:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **David Cottrell:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

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Formal ethical approval for the project was provided by the University of Leeds, Faculty of Medicine & Health Ethics Committee (MREC 18-098).

Data Sharing: Data sharing is subject to original study author permissions.

Professor Richard Riley served as the statistical expert for this research and reviewed the statistical analysis plan. The project was peer reviewed as part of the grant application and protocol publication.

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