

Non-pharmacological and pharmacological interventions for the reduction or prevention of topographies of behaviours that challenge in people with intellectual disabilities

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Non-pharmacological and pharmacological interventions for the reduction or prevention of topographies of behaviours that challenge in people with intellectual disabilities: a systematic review and meta-analysis of randomised controlled trials



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Summary

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Background People with intellectual disability show a high prevalence of behaviours that challenge. Clinical guidelines recommend that such behaviour should first be treated with non-pharmacological interventions, but research suggests off-label pharmaceuticals are commonly used. We aimed to evaluate the efficacy of non-pharmacological and pharmacological interventions for topographies of behaviours that challenge drawn from randomised controlled trials (RCTs).

Methods In this systematic review and meta-analysis, we searched PsycINFO, MEDLINE, Embase, CINAHL, and CENTRAL databases for RCT studies assessing an intervention (pharmacological or non-pharmacological) for behaviours that challenge (self-injury behaviour, aggression, destruction of property, irritability, and a composite overall measure) in participants with intellectual disability. The primary aim was to assess the efficacy of non-pharmacological and pharmacological interventions on behaviours that challenge. Secondary aims were to evaluate how effects varied over time and whether intervention, methodological, and participant characteristics moderate efficacy. We extracted standard mean difference (SMD) effect sizes (Cohen's *d*) from eligible studies and meta-analysed the data using a series of random effects models and subgroup analyses. This study was registered with PROSPERO 2021, CRD4202124997.

Findings Of 11912 reports identified, 82 studies were included. 42 (51%) studies assessed non-pharmacological interventions and 40 (49%) assessed pharmacological interventions. Across all studies, 4637 people with intellectual disability aged 1–84 years (mean age 17.2 years) were included. 2873 (68.2%) were male, 1339 (28.9%) were female, and for 425 (9.2%) individuals, data on gender were not available. Data on ethnicity were unavailable. Small intervention effects were found for overall behaviours that challenge at post-intervention (SMD -0.422 , 95% CI -0.565 to -0.279), overall behaviours that challenge at follow-up (-0.324 , -0.551 to -0.097), self-injury behaviour at post-intervention (-0.238 , -0.453 to -0.023), aggression at post-intervention (-0.438 , -0.566 to -0.309), and irritability at post-intervention (-0.255 , -0.484 to -0.026). No significant differences between non-pharmacological and pharmacological interventions were found for any topography of behaviours that challenge (all $p > 0.05$).

Interpretation A broad range of interventions for behaviours that challenge are efficacious with small effect sizes for people with intellectual disability. These findings highlight the importance of precision in the measurement of behaviours that challenge, and when operationalising intervention components and dosages.

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Introduction

Approximately 1% of the general population have an intellectual disability,¹ of whom 10–15% show behaviours that challenge (BtC).^{2,3} The term BtC is used to describe behaviours that present difficulties to individuals, caregivers, and education and health-care services.^{2,3} Examples of these behaviours are self-injury, aggression, or destruction of property.^{2,3} Given the negative outcomes of BtC to the individual and systems around them,^{4,5} it is crucial that effective interventions are available.^{6,7} A broad

range of non-pharmacological and pharmacological interventions are recommended for the reduction of BtC,^{6,7} with previous meta-analyses reporting moderate effect sizes for these; although null findings and small effects are also described.^{8–13}

The guidelines of the UK National Institute for Health and Care Excellence (NICE) recommend initially offering non-pharmacological interventions, with medication used only when risk of harm from BtC is severe or when non-pharmacological interventions are

Research in context

Evidence before this study

We searched PsycINFO, MEDLINE, Embase, CINAHL, and CENTRAL databases for articles (including original research and systematic reviews and meta-analyses) in English exploring the effectiveness of pharmacological and non-pharmacological interventions for individuals with intellectual disability with behaviours that challenge on Dec 6, 2019. Four sets of terms allowed for a search of ["behaviours that challenge"] AND ["intellectual disability" OR "autism"] AND ["intervention"]; alternative descriptors were included. From this search, systematic reviews and meta-analyses exploring the effectiveness of pharmacological and non-pharmacological interventions were identified. Generally, existing systematic reviews and meta-analyses were restricted in their focus, for example, some reviews considered only interventions for specific behaviours such as aggressive behaviour or self-injury. Other reviews were restricted by intervention type (eg, reviewing only non-pharmacological or pharmacological interventions or one specific form of intervention such as parent training programmes or risperidone). Only two meta-analyses examined the effectiveness of interventions across both pharmacological and non-pharmacological interventions for multiple topographies of behaviours: these studies did not focus on randomised controlled trials (RCTs).

Added value of this study

To our knowledge, this is the first meta-analysis to explore the effectiveness of pharmacological and non-pharmacological interventions for multiple topographies of behaviours that challenge in people with intellectual disability, drawing only on RCT studies. The results showed small intervention effects for all topographies of behaviour, with no significant differences identified between non-pharmacological and pharmacological interventions.

Implications of all the available evidence

These findings suggest that a broad range of interventions for behaviours that challenge are efficacious for people with intellectual disability. Given the lack of significant differences between non-pharmacological and pharmacological interventions, services should consider carefully which interventions are most appropriate for supporting individuals with intellectual disability who show behaviours that challenge. To inform these decisions, clinicians are encouraged to draw on existing guidance such as NICE guidelines. Further research is required to increase understanding of which interventions are most effective for specific behaviours in people with intellectual disability.

ineffective.⁷ Despite these guidelines and the efficacy of non-pharmacological interventions,^{8,10,11} off-label medication prescription and polypharmacy are common.^{14,15} In some cases, medication is used inappropriately as the primary response to BtC,^{16–18} which contravenes clinical guidance, and might lack efficacy due to significant side-effects and poorer long-term outcomes.^{9,13,19,20} Several initiatives have been published encouraging clinicians to review and, where appropriate, discontinue medication use for BtC (eg, stopping overmedication of people with a learning disability, autism, or both [STOMP]).²¹ Barriers to discontinuing medication include concerns that BtC might re-emerge or worsen after medication discontinuation,^{14,22} alluding to a lack of clinical confidence in the effectiveness of non-pharmacological interventions. Direct comparison of the efficacies of non-pharmacological and pharmacological interventions is essential to provide clinicians with a holistic overview of the literature to guide service provision and patient care. The few meta-analyses that compared pharmacological and non-pharmacological interventions showed no significant differences in efficacy, but these conclusions were limited by the inclusion of small samples and of uncontrolled quasi-experimental and naturalistic studies.^{10,11} Several randomised controlled trials (RCTs) have been published in recent years, and therefore, review of these studies comparing non-pharmacological and pharmacological interventions is warranted.

NICE also suggests that preventive interventions should be delivered to individuals at high risk of, or with, emergent BtC, alongside interventions for which BtC are not the primary target.⁷ For example, pain, poor sleep, and low mood might increase the emergence or maintenance of BtC,^{23,24} with interventions for these crucial areas conferring downstream benefits for these behaviours. Generally, these types of interventions are excluded from reviews and therefore missed or evaluated in isolation from the rest of the published literature.^{8,10,11,13,25} There is a need to collate these data within one review to explore whether intervention target moderates intervention efficacy.

Previous meta-analyses have examined how intervention characteristics affect efficacy. Pharmacological interventions can be categorised into medication classes, with antipsychotics reported to show the largest treatment effects.¹³ However, categorising non-pharmacological interventions is challenging, and previous meta-analyses have adopted varying approaches.^{8,10,11} These studies reported greater treatment effects for interventions that manipulated antecedents¹¹ and for those that combined mindfulness and behavioural techniques.⁸ Replication of these findings is hampered by a lack of detail and consistency in study descriptions of intervention components. A complementary, pragmatic approach is to categorise interventions on objective characteristics, such as treatment duration, delivery mode, and recipient.^{11,12,26} Evaluation of these characteristics would be highly

informative for clinicians to understand and translate the parameters of effective interventions.

Methodological characteristics, such as RCT design, assessment timepoint (post-intervention, follow-up) and type of comparison group, might also moderate intervention efficacy. Reviews of non-pharmacological interventions found no significant associations between assessment timepoint and outcome,^{8,10,11} suggesting that intervention effects are maintained over time. However, it is necessary to establish if this is the case when only RCT studies are appraised. Participant characteristics, such as gender or sex, chronological age, and level of ability, might also moderate efficacy. Previous meta-analyses have indicated no clear association between treatment effects and participant characteristics,^{8,10,11} but they might have been limited by the number and design of studies included.

Finally, intervention efficacy can differ across topographies of BtC. BtC is a broad term encapsulating many behaviours, from self-injury behaviour, to sleep problems, to irritability.²⁷ This lack of specificity is problematic, as outcome measures for BtC refer to behaviours with varying underlying mechanisms that might require different interventions.²⁷ For example, although pain might act as a setting event for all BtC,^{24,28} it might be a unique antecedent to self-injury behaviour.^{29,30} Thus, reviews should be specific about the target BtC being evaluated. Self-injury, aggression, and property destruction are BtC of particular interest, given these are most concerning to families and health-care, education, and care staff.³¹ Irritability and overall BtC, as measured by total scores on common measures of BtC, are important given that these are considered key BtC intervention targets and are frequently reported within the pharmacological and non-pharmacological treatment literature.

The aims of this review were to: (1) establish the efficacy of non-pharmacological and pharmacological interventions on self-injury, aggression, destruction of property, irritability, and overall BtC (total BtC scores) in people with intellectual disability; (2) determine how these effects vary over time through the analysis of post-intervention timepoints and long-term follow-up; and (3) explore how study, participant, and intervention characteristics moderate efficacy.

Methods

Search strategy and selection criteria

Title, abstract, and keyword search of electronic databases was conducted on Dec 6, 2019, and updated on June 14, 2022, using PsycINFO (from 1967), MEDLINE (from 1946), Embase (from 1974), CINAHL (from 1975), and the Cochrane Central Register of Controlled Trials (CENTRAL; appendix pp 5–7). We also searched the reference lists of relevant articles and previous reviews. The search strategy combined four sets of terms with alternative descriptors

incorporated (full search terms are in the appendix, p 5): ["behaviours that challenge"] AND ["intellectual disability" OR "autism"] AND ["intervention"]. Although this review focused on people with intellectual disability who might or might not be autistic, autism terms were included due to concerns that people with intellectual disability might be missed when authors presented autism as the primary diagnosis in the sample. We excluded papers of studies of autistic participants without intellectual disability.

The review included individuals of any age with intellectual disability (operationalised as intelligence quotient [IQ] <70). We included studies of participants with an IQ in the normal range (IQ ≥71) if they presented an isolated analysis of people with intellectual disability (identified post-randomisation) or if less than 10% of the analysed sample had an IQ higher than 70. Studies recruiting individuals at risk of developmental delay were included to appraise efficacy of preventive interventions. Eligible studies included those evaluating an intervention in which BtC were assessed as the primary or secondary outcome. Eligible BtC outcomes were self-injury, aggression, property destruction, irritability, or overall BtC (total BtC score). To be eligible, studies had to use an RCT design (minimum of two groups), and their findings had to be available in English.

One reviewer (LG) conducted screening and selection for all articles. A second reviewer (AH) independently conducted screening and selection for 2875 (24.1%) of studies. Where discrepancies were identified, consensus discussions were undertaken. Inter-rater reliability was good (Cohen's κ 0.628) with 97.4% agreement. Quality review was conducted by LG using the Cochrane risk assessment of bias tool (RoB2) to calculate a quality index.³² Interrater reliability, which was conducted by AH on 21 (25.6%) studies, was moderate to excellent (Cohen's κ 0.632–0.842).

Data analysis

To establish the efficacy of non-pharmacological and pharmacological interventions on BtC and to determine how these effects vary over time, we extracted standard mean difference (SMD) effect sizes (Cohen's d) from eligible studies. We calculated effect sizes from means and SDs comparing experimental and comparison groups at post-intervention or follow-up. When these data were not provided, we contacted the authors of the papers. When contact was unsuccessful, we calculated effect sizes from test statistics, reported effect sizes, or p values. Effect sizes were coded for inclusion in one of ten analyses: one meta-analysis for each of the two timepoints of interest (post-intervention, follow-up) for each of the five behaviours of interest (self-injury, aggression, property destruction, and irritability, and overall BtC). The process of selecting outcome measures is reported in the appendix (p 8). When the number of included effects was 3 or less, results were not reported.

See Online for appendix

A sufficient number of effects was reported for five of the planned ten meta-analytic models: overall BtC (post-intervention), overall BtC (follow-up), self-injury (post-intervention), aggression (post-intervention), and irritability (post-intervention). Consistent with previous guidance, effect sizes were interpreted as small (0.2), medium (0.5), and large (0.8).³³

We adopted the generic inverse variance approach using random effects models to allow for between-studies differences in the true underlying effect. We used the DerSimonian-Laird estimator, since QQ plots using this model indicated an approximately normal distribution of effects (appendix pp 9–11). We assessed the impact of disproportionately influential studies using “leave-one-out” analyses and studies showing marked contribution to the overall effect, and heterogeneity were reviewed and removed from the meta-analysis if necessary (appendix pp 12–16).

To explore how study, participant, and intervention characteristics moderate efficacy, we performed a series of subgroup analyses and meta-regressions between BtC outcomes and study quality, methodological, participant, and intervention characteristics. For study quality, we used individual RoB2 criteria ratings to determine associations between risk of bias and intervention effect sizes. Methodological characteristics were: type of comparison group (waitlist, treatment as usual, placebo, active control), study design (simple RCT, cluster, crossover, discontinuation), and assessment timepoint (in weeks for post-intervention and follow-up assessments). Participant characteristics were: percentage of male participants, mean chronological age, and level of ability (percentage of individuals labelled as having a severe to profound intellectual disability, or the sample mean IQ score). Intervention characteristics were: intervention type (non-pharmacological, pharmacological), pharmacological medication type (antiepileptics, antipsychotics, other), non-pharmacological delivery mechanism (group, individual), non-pharmacological recipient (individual, parent, care staff, combination), and intervention target (prevention of BtC, reduction of BtC, BtC not primary target).

Heterogeneity was assessed using Higgin's I^2 with greater values indicating more heterogeneity. Substantial heterogeneity was defined as an I^2 value greater than 75%.³⁴ Publication bias was evaluated by visual inspection of funnel plots and Egger and colleagues' test of asymmetry.³⁵ If publication bias is identified, then a trim and fill procedure³⁶ will be undertaken. This study was registered with PROSPERO 2021, CRD4202124997.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The search yielded 11912 records, with 82 studies reporting on 125 effects meeting inclusion (figure 1; appendix pp 21–31). All studies included a post-intervention timepoint (baseline to post-intervention: median 12 weeks, range 1–104) with 14 (17%) including at least one additional follow-up timepoint (median 36 weeks, range 12–130). Treatment as usual was used as a comparison in 21 (26%) studies, eight (10%) used waitlist, 42 (51%) placebo condition, and 11 (13%) active control. The countries that each study was conducted in are displayed in the appendix (pp 21–31).

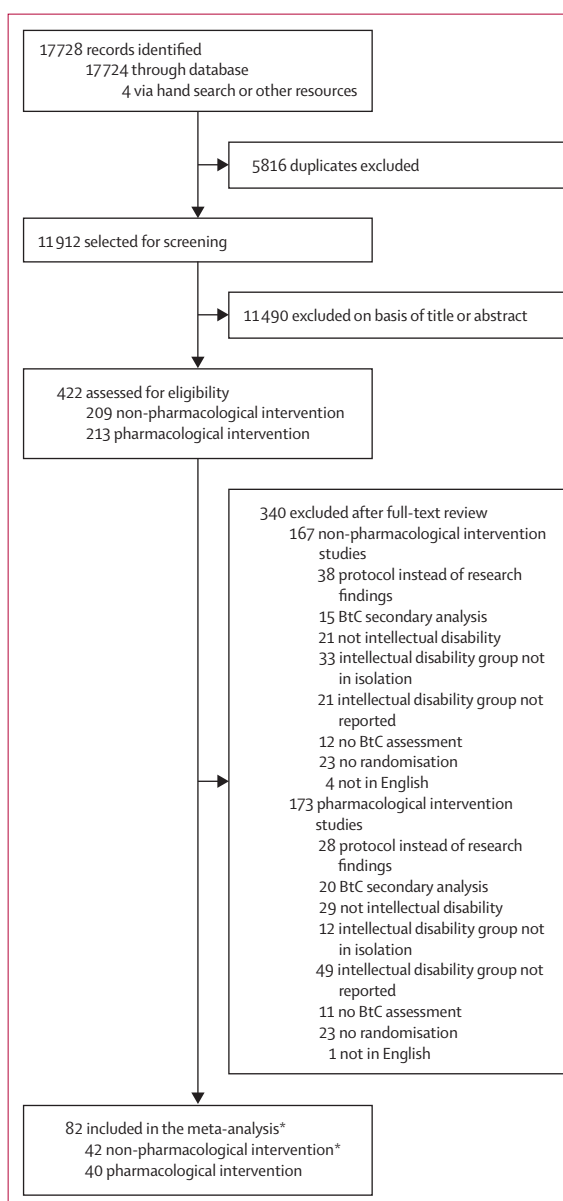


Figure 1: Study selection

BtC=behaviours that challenge. *One article counted twice as it reported on two separate studies.

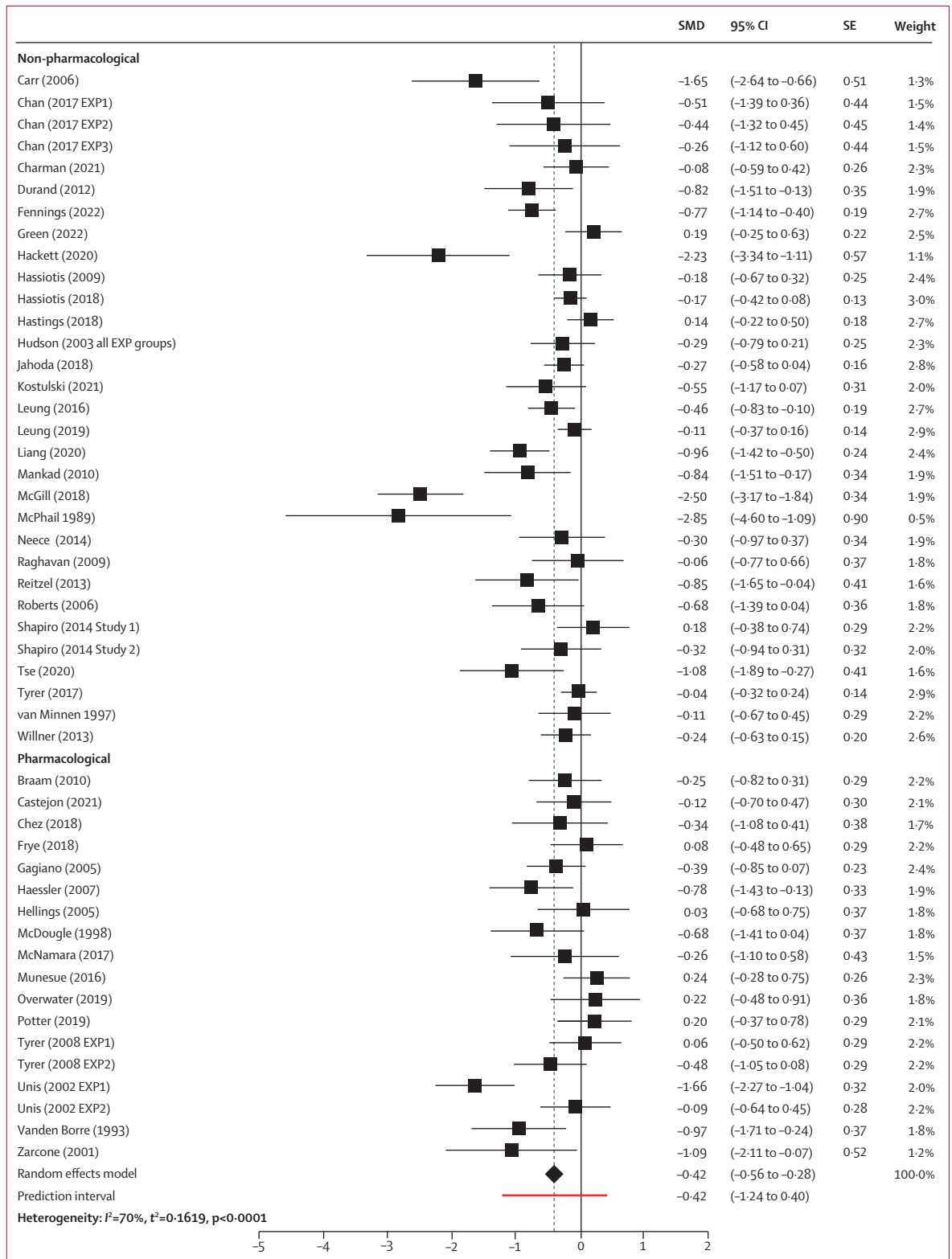


Figure 2: Forest plot for post-intervention total BtC scores (overall BtC)
 BtC=behaviours that challenge. EXP=experimental group. SE=standard error. SMD=standard mean difference.

63 (77%) studies reported interventions to reduce BtC, four (5%) to prevent BtC, and 15 (18%) were studies in which BtC was not the primary target. 42 (51%) studies assessed non-pharmacological interventions and 40 (49%) assessed pharmacological interventions. Of the 42 studies assessing non-pharmacological interventions, 13 (31%) assessed a manualised intervention for parents, six (14%) assessed care staff interventions drawing on behavioural and systemic approaches, four (10%) evaluated CBT-based packages, and four (10%) examined relaxation or mindfulness-based interventions. The remaining 15 (36%) reported on a mix of other non-pharmacological interventions. Pharmacological interventions included three types of medication: antipsychotics ($k=16$, 41%; most common being risperidone), antiepileptics ($k=5$, 13%), and other types ($k=20$, 50%).

Across all studies, 4637 people with intellectual disability were included. Of these, 2873 (68.2%) were male and 1339 (28.9%) were female. Eight studies did not describe the gender of their participants so data for 425 (9.2%) individuals are not available. The age range of participants was 1–84 years (mean age 17.2 years); assuming no overlap. Ethnicity data were not available because of limited reporting. 28 (34%) studies described a proportion of their sample as having a severe or profound intellectual disability (median proportion of participants with severe or profound intellectual disability was 53.3%) with 32 (39%) studies reporting that a proportion of their sample had a mild or moderate intellectual disability (median proportion of participants with mild or moderate intellectual disability was 60.0%). 26 (32%) studies reported IQ scores rather than intellectual disability classifications (average IQ median 55.7, range 11.5–68.0). 22 (27%) studies did not comment on the level of ability.

The full findings of random effects meta-analyses and subgroup analyses and meta-regressions on

methodological, participant, and intervention characteristics are available in the appendix (pp 32–39).

For overall BtC (post-intervention), 45 studies reporting 49 effects met the inclusion criteria. The random effects model indicated a small intervention effect (SMD -0.422 , 95% CI -0.565 to -0.279 ; figure 2). Moderate heterogeneity was reported ($I^2=69.7\%$, 95% CI 59.5 to 77.4; $\tau^2=0.162$; $p<0.0001$). A significant difference between RoB2 subgroups was identified for a selection of reported results ($\chi^2=14.01$; $p<0.001$) such that studies rated as “low” risk had lower effect sizes (SMD -0.103 , 95% CI 0.247 to 0.332, $\tau^2=0.010$) than did studies rated as “some concerns” (-0.539 , -0.747 to -0.042 , $\tau^2=0.231$) and “high” risk (-0.555 , -0.916 to -0.194 , $\tau^2=0.128$). All other subgroup analyses of quality criteria were not significant ($p>0.05$; appendix p 32). Subgroup analyses of moderators revealed an effect for intervention target such that studies aiming to reduce behaviour showed a greater SMD (-0.548 , 95% CI -0.737 to -0.359 , $\tau^2=0.197$) than did interventions for prevention or other targets (SMD -0.193 , 95% CI -0.444 to 0.057, $\tau^2=0.177$ and SMD -0.218 , 95% CI -0.510 to 0.075, $\tau^2=0.021$; $\chi^2=6.33$, $p=0.042$). All other subgroup analyses were not significant ($p>0.05$; appendix p 34).

Statistical analysis of publication bias indicated that possible bias was present ($t=-3.38$, $p=0.001$). The funnel plot (appendix p 39) indicated there was a high proportion of papers showing effect sizes indicative of the null hypothesis. The trim and fill procedure yielded a corrected random effects model with an SMD of -0.449 (95% CI -0.582 to -0.295), a 4.1% increase in the uncorrected estimate. Because of the substantial level of heterogeneity present, these results should be interpreted with caution.

For BtC (follow-up), nine studies ($k=9$) met the inclusion criteria, eight of which were of non-pharmacological interventions. A small intervention effect (SMD -0.324 ,

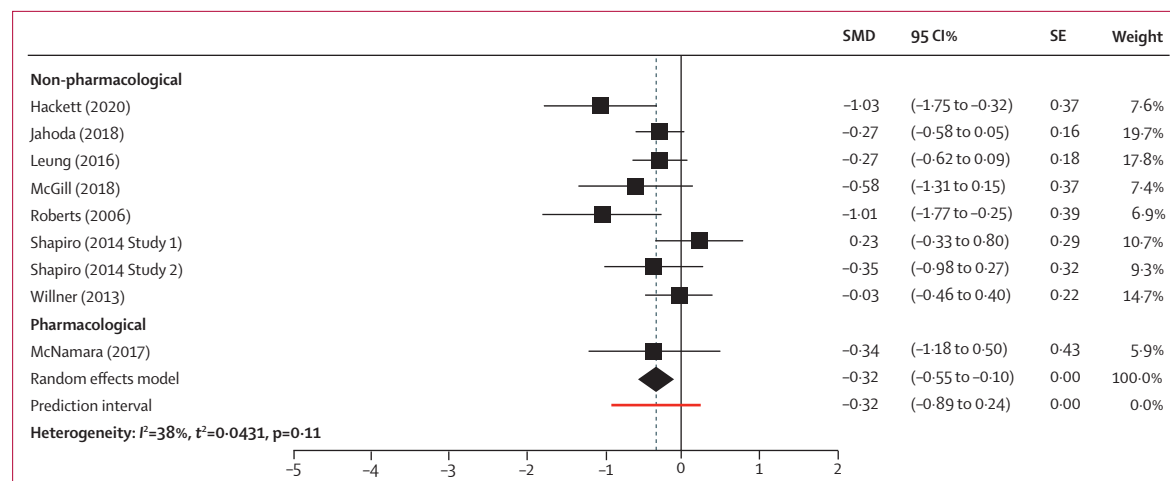


Figure 3: Forest plot for follow-up total BtC scores (overall BtC)
BtC=behaviours that challenge. SE=standard error. SMD=standard mean difference.

95% CI -0.551 to -0.097 ; figure 3) with low heterogeneity was identified ($I^2=38.4\%$, 95% CI 0.0 to 71.7 ; $\tau^2=0.043$; $p=0.11$). Subgroup analyses of RoB2 criteria were not significant (appendix p 32). We did not do subgroup analyses for intervention type, medication type, or participant ability because of insufficient data. Analyses of intervention target were significant, with greater effects obtained with interventions aiming to reduce BtC behaviour (SMD -0.765 , 95% CI -1.144 to -0.386 , $\tau^2=0$) than with interventions for prevention of BtC or other targets (-0.154 , -0.477 to 0.169 , $\tau^2=0.020$ and -0.186 , -0.438 to 0.166 , $\tau^2=0$; $\chi^2=7.36$, $p=0.025$). All other subgroup analyses were not significant ($p>0.05$; appendix p 35). Statistical analysis of publication bias could not be calculated as the number of effects was low ($k<10$).

For self-injury behaviour (post-intervention), 12 studies ($k=14$) met the inclusion criteria. The random effects model indicated a small effect size (SMD -0.238 , 95% CI -0.453 to -0.023 ; figure 4) with low heterogeneity reported ($I^2=26.6\%$, 95% CI 0.0 to 61.2 ; $\tau^2=0.041$; $p=0.17$). Subgroup analyses using RoB2 criteria showed no significant differences (appendix p 33). Due to insufficient effects, subgroup analyses were not calculated for non-pharmacological delivery, non-pharmacological recipient, intervention target, or mean IQ score. No significant subgroup analyses were identified ($p>0.05$; appendix p 36) and no significant publication bias was reported ($t=-1.96$, $p=0.074$).

For aggression (post-intervention), 22 studies ($k=26$) met inclusion criteria. The random effects model showed a small intervention effect (SMD -0.438 , 95% CI -0.566 to -0.309 ; figure 5) with significant,

moderate heterogeneity ($I^2=53.9\%$, 95% CI 28.2 to 70.6 ; $\tau^2=0.133$; $p<0.0001$). No RoB2 criterion was associated with aggression outcomes ($p>0.05$; appendix p 33).

Significant differences for subgroup analyses of study design were identified, with cluster RCTs showing smaller SMDs than simple RCT designs ($\chi^2=7.56$, $p=0.023$). A significant association was identified for pharmacological medication type, with antipsychotics (SMD -0.549 , 95% CI -0.983 to -0.115 , $\tau^2=0.249$) and non-pharmacological interventions (SMD -0.495 , -1.050 to -0.301 , $\tau^2=0.064$) showing larger effects than other medications (0.107 , -0.328 to 0.542 , $\tau^2=0$; $\chi^2=6.30$, $p=0.043$). We could not do subgroup analyses of intervention target because of insufficient data. For all other subgroups, no significant associations were identified ($p>0.05$; appendix p 37) and no significant publication bias was shown ($t=-0.92$, $p=0.37$). These results should be interpreted with caution because of heterogeneity.

For irritability (post-intervention), 25 studies ($k=27$) met the inclusion criteria. Of note, 24 of the 27 effects were pharmacological interventions. The random effects model showed a small effect (SMD -0.255 , 95% CI -0.484 to -0.026 ; figure 6) with moderate heterogeneity ($I^2=72.2\%$, 95% CI 59.1 to 81.0 ; $\tau=0.243$; $p<0.0001$). No RoB2 criterion was associated with irritability outcomes (appendix p 33). Significant differences for mean IQ level were identified ($\beta=-0.02$, standard error 0.01 , $\tau^2=0.218$, $p=0.018$) such that larger effects were reported for studies with samples with higher mean IQs. No other significant differences were identified in the subgroup analyses ($p>0.05$; appendix p 38) and no significant publication bias was

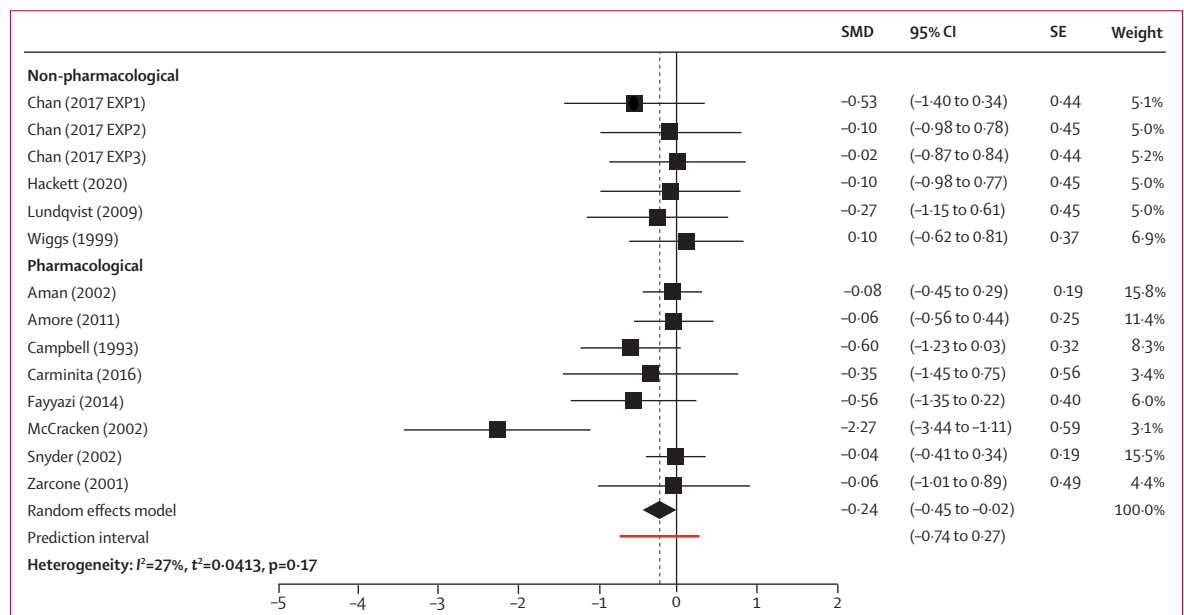


Figure 4: Forest plot for post-intervention self-injury behaviour scores. EXP=experimental group. SE=standard error. SMD=standard mean difference.

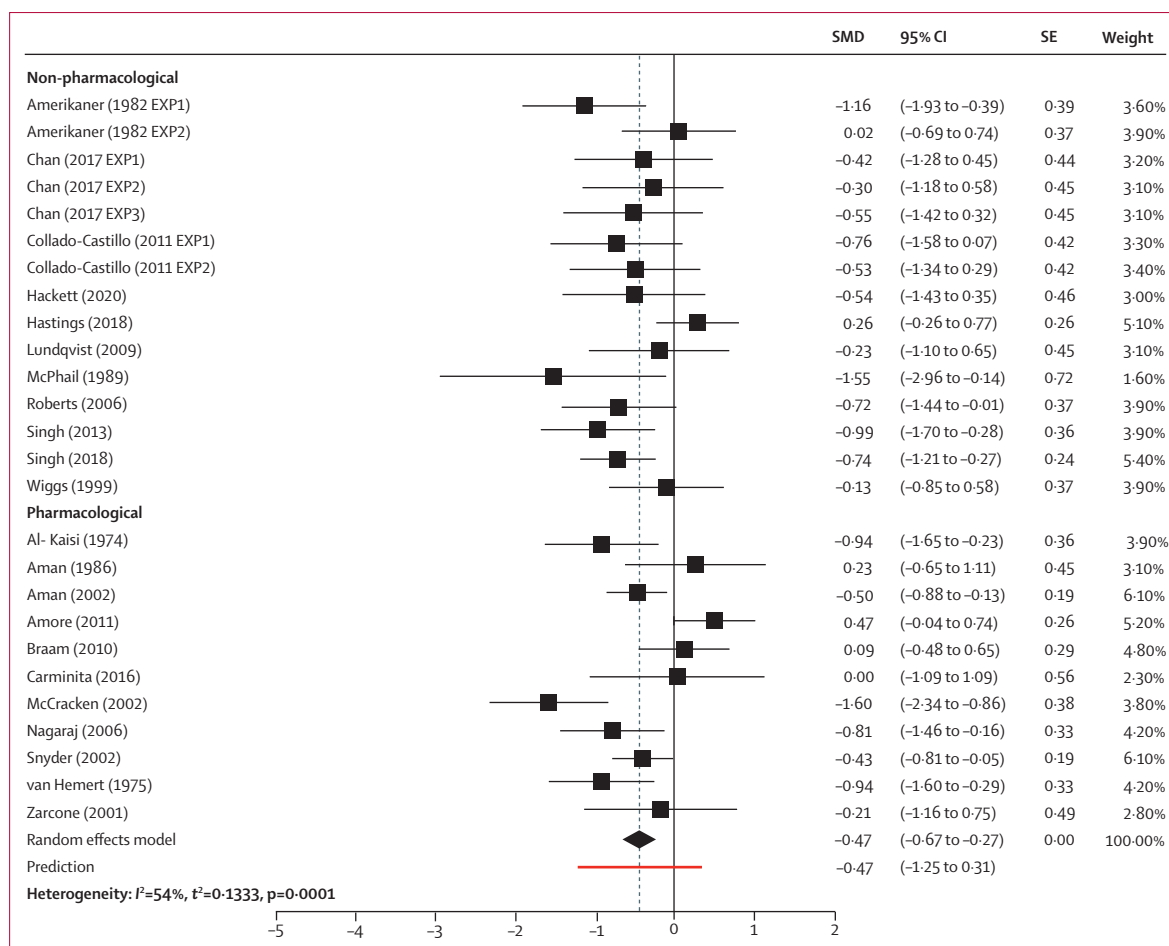


Figure 5: Forest plot for post-intervention aggression scores
EXP=experimental group. SE=standard error. SMD=standard mean difference.

shown ($t=1.61$, $p=0.12$). These results should be interpreted with caution because of heterogeneity.

Discussion

To our knowledge, this is the first meta-analysis to combine examination of both non-pharmacological and pharmacological RCT interventions for the reduction or prevention of BtC in people with intellectual disability. This review expanded on the current literature by evaluating novel moderators of intervention efficacy, including study design, comparison group, and most notably, intervention target.

Consistent with previous reviews, the random effects models revealed a small intervention effect for all BtC,^{8,10–13} extending previous reviews by showing that the effect remains when only RCTs are included. Overall BtC (post-intervention) outcomes were associated with the RoB2 selection of reported result, suggesting that larger intervention effects might have been affected by poor methodology, rather than reflecting true efficacy. However, RoB2 ratings of “high” risk or “some concerns” were often assigned due to insufficient reporting detail

rather than definitive risk of bias. Thus, future studies should improve reporting and adopt open science practices to facilitate evaluation of the impact of methodological bias on intervention efficacy.

Similarly, we showed that previous review findings of no significant differences between non-pharmacological and pharmacological interventions across BtC outcomes^{10,11} persist when only RCTs are evaluated. Also replicating previous findings, antipsychotics had the largest effect on aggression relative to other medication types,¹³ suggesting that antipsychotics might be efficacious for only aggression and not for other topographies of BtC. Importantly, the effect size for antipsychotics was similar to those found for non-pharmacological interventions, providing empirical support for clinical guidance that non-pharmacological interventions led by multi-disciplinary teams should be the primary response to BtC.⁷ These data also support service engagement in initiatives, such as STOMP, and UK Royal College of Psychiatrists guidance²¹ to reduce the number of individuals prescribed antipsychotics for BtC.

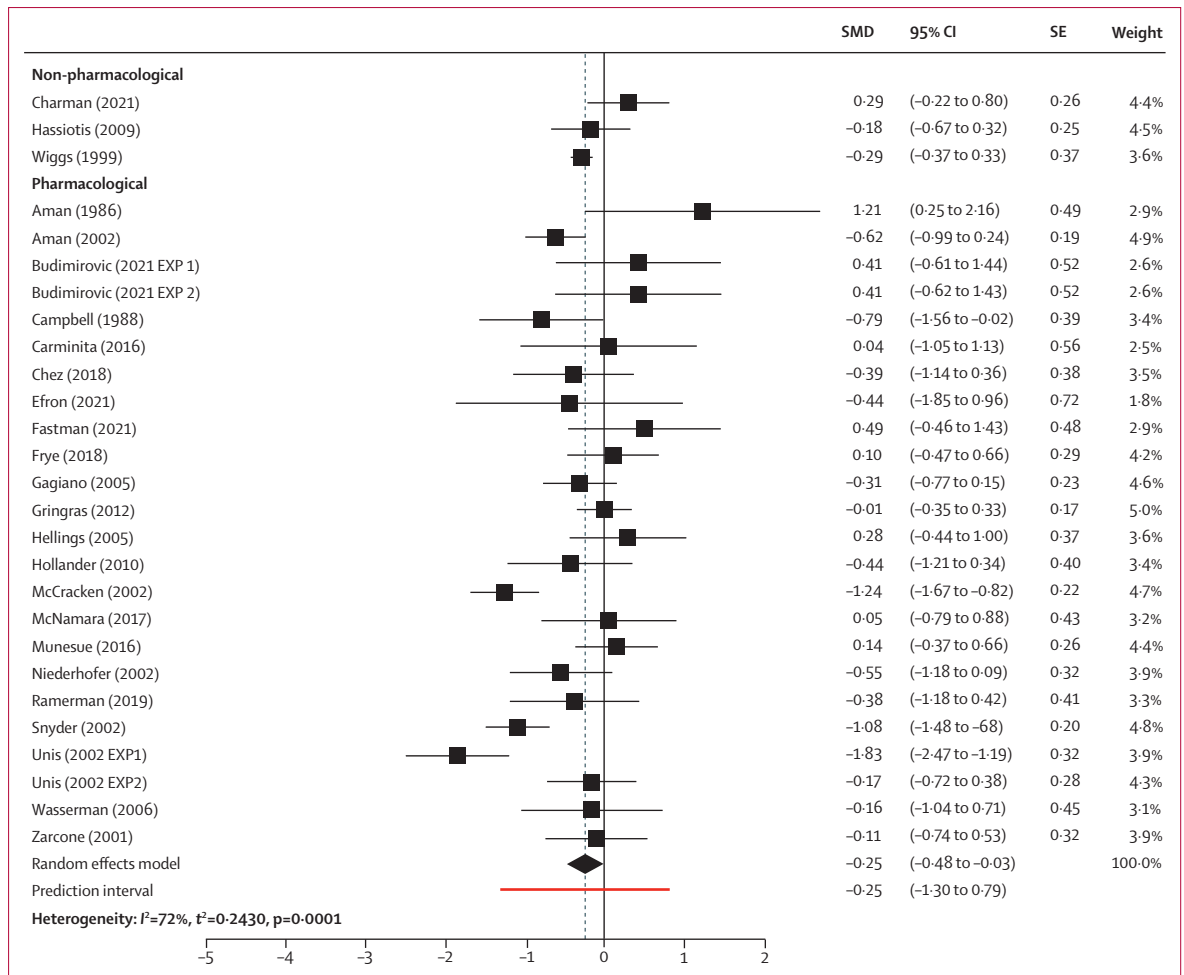


Figure 6: Forest plot for post-intervention irritability scores
EXP=experimental group. SE=standard error. SMD=standard mean difference.

Subgroup analyses of non-pharmacological intervention components were not significant. Intervention target was associated with intervention efficacy for overall BtC at both post-intervention and follow-up timepoints, such that interventions to reduce BtC were more efficacious than those to prevent BtC or addressing other targets. However, this result should be interpreted with caution as the number of effects for other targets was low. Furthermore, in preventive interventions, it is likely that individuals were showing no BtC or low frequency or severity of BtC at baseline, which makes these studies vulnerable to floor effects. As such, a result of no change after intervention might still be considered successful, since BtC has not emerged or worsened. Future RCTs of preventive interventions would benefit from assessing long-term follow-up or other indicators of efficacy (eg, parental or caregiver self-efficacy or knowledge of preventing BtC).

Given the paucity of intervention characteristics associated with treatment efficacy, clinicians might consider other factors in guiding intervention provision,

such as maintenance of treatment effects. In this meta-analysis, few studies reported follow-up data. For overall BtC (follow-up), we obtained a small effect size, which was similar to that reported for overall BtC (post-intervention), suggesting effect maintenance. Other variables with the potential to guide intervention selection are cost-effectiveness, side-effects, and intervention acceptability. Pharmacological interventions can be associated with notable side-effects,^{9,13,20} however, non-pharmacological studies rarely report harms,³⁷ making clinical recommendations based on side-effects somewhat challenging. Finally, interventions rarely report acceptability, which could guide intervention delivery, and be used to optimise engagement. Future studies should incorporate these outcomes to improve the evidence base and allow exploration of the influence of these factors on intervention efficacy and uptake.

Of the methodological characteristics, only study design was associated with BtC outcomes. Specifically, for aggression (post-intervention), cluster RCT designs

had lower effect sizes than did simple RCT designs. The number of effects in this analysis was low, and so findings should be interpreted with caution. Inspection of study characteristics and quality indicated no clear explanation of the results (further interpretation in appendix p 40). Finally, higher IQ was associated with better outcomes for irritability. However, irritability is a transdiagnostic symptom and is primarily conceptualised as a mood dysregulation, which might or might not be accompanied by behavioural outbursts.³⁸ These behavioural manifestations lack specificity and, as irritability is conceptualised as a dysregulation of mood, there is a clear cognitive component to this construct.^{38,39} Correspondingly, irritability is negatively associated with age.⁴⁰ Thus, individuals with lower developmental ability might be more likely to score high on measures of irritability because of lower cognitive resources. As such, irritability as a BtC outcome might reflect the cognitive capacity of the individual to regulate their mood, rather than an observable behaviour. Since more able individuals have more cognitive resources to regulate their mood than less able individuals, assessment of this construct for intervention efficacy would favour these more able individuals. Future studies should seek to understand this relationship and consider introducing more precision in the assessment of BtC to clearly define observable behaviours, rather than internal states of mood. Greater consideration could be given to the appropriate selection of interventions that address the underlying mechanisms of constructs. For example, an intervention for irritability with a cognitive rather than behavioural approach might be most appropriate.

A key strength of this meta-analysis was the careful attention to the categorisation of individual topographies of BtC. Similar to irritability, overall BtC might be problematic given the wide variety of included behaviours.²⁷ This variability might explain why we identified only one significant moderator (intervention target) for overall BtC, despite this being the analysis with the greatest statistical power. Measures assessing one construct of BtC in isolation were less common, with this being particularly striking for property destruction ($k=2$). The paucity of literature for individual BtC is concerning, given the deleterious impacts of these behaviours. Future studies should include precise measures of specific behaviours to explore the efficacy of interventions and improve evidence-based practice.

There are some limitations to this meta-analysis. The first pertains to the quality of the data. Ethnicity data were not extracted as part of this meta-analysis although, notably, these data were not supplied by some studies. We were not able to perform analyses comparing gender differences or the type and content of the non-pharmacological interventions because of limited reporting and data. Not all studies reported on the

interventions participants were receiving as part of treatment as usual. Thus, there could have been interactions that mediated the efficacy of the intervention under assessment. Because of the small number of included studies and high variability in medication types and dosages, only broad examination of medication class was possible. Additionally, few studies explored the effectiveness of combined non-pharmacological and non-pharmacological interventions. Second, although we explored associations between moderators of interest and BtC outcomes, we could not investigate interactions between multiple moderators because of insufficient eligible effects. Finally, key variables not included here might have moderated results.

This review highlights that the evidence base, while of a moderate size, remains small and underpowered when intervention, methodological, participant, and BtC characteristics are considered. Future studies should improve reporting of these characteristics and use greater precision in measures of BtC, as well as clearly operationalised intervention components and dosages. There is also a need for more research in which participant and intervention characteristics are systematically addressed to identify which people might benefit from what types of intervention. Such evidence is necessary to inform clinicians and services in their provision of person-centred care.

In conclusion, this meta-analysis has highlighted efficacious interventions for managing BtC shown by people with intellectual disability, with small effect sizes. Crucially, no significant differences were shown between pharmacological and non-pharmacological interventions for any type of BtC.

Contributors

LG and CR conceptualised the study, and LG, CR, and AW contributed to the study design. LG conducted the literature search and data collection. AH also conducted part of the literature screening and data collection for reliability purposes. LG, CR, CJ, and AW had access to the raw data, verified and analysed it. LG, CR, and AW did the data interpretation. All authors helped to write the paper. LG had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests. CR has received research grants from the Cerebra Charity, Medical Research Council, and Baily Thomas Charitable Fund.

Data sharing

The data that support the findings of this review are available on reasonable request to the corresponding author.

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