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# Cognitive behavioural therapy with exposure and response prevention in the treatment of obsessive-compulsive disorder: A systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

*Background:* Cognitive behavioural therapy (CBT), incorporating exposure and response prevention (ERP) is widely recognised as the psychological treatment of choice for obsessive-compulsive disorder (OCD). Uncertainty remains however about the magnitude of the effect of CBT with ERP and the impact of moderating factors in patients with OCD.

*Method:* This systematic review and meta-analysis assessed randomised-controlled trials of CBT with ERP in patients of all ages with OCD. The study was preregistered in PROSPERO (CRD42019122311). The primary outcome was end-of-trial OCD symptom scores. The moderating effects of patient-related and study-related factors including type of control intervention and risk of bias were examined. Additional exploratory analyses assessed the effects of treatment fidelity and impact of researcher allegiance.

*Results:* Thirty-six studies were included, involving 2020 patients (537 children/adolescents and 1483 adults) with 1005 assigned to CBT with ERP and 1015 to control conditions. When compared against all control conditions, a large pooled effect size (ES) emerged in favour of CBT with ERP ($g = 0.74$: 95% CI = 0.51 to 0.97 $k = 36$), which appeared to diminish with increasing age. While CBT with ERP was more effective than psychological placebo ($g = 1.13$ 95% CI 0.71 to 1.55, $k = 10$), it was no more effective than other active forms of psychological therapy ($g = -0.05$: 95% CI −0.27 to 0.16, $k = 8$). Similarly, whereas CBT with ERP was significantly superior when compared to all forms of pharmacological treatment ($g = 0.36$: 95% CI 0.7 to 0.64, $k = 7$), the effect became marginal when compared with adequate dosages of pharmacotherapy for OCD ($g = 0.32$: 95% CI −0.00 to 0.64, $k = 6$).A minority of studies ($k = 8$) were deemed to be at low risk of bias. Moreover, three quarters of studies ($k = 28$) demonstrated suspected researcher allegiance and these studies reported a large ES ($g = 0.95$: 95% CI 0.69 to 1.2), while those without suspected researcher allegiance ($k = 8$) indicated that CBT with ERP was not efficacious ($g = 0.02$: 95% CI −0.29 to 0.33).

*Conclusions:* A large effect size was found for CBT with ERP in reducing the symptoms of OCD, but depends upon the choice of comparator control. This meta-analysis also highlights concerns about the methodological rigor and reporting of published studies of CBT with ERP in OCD. In particular, efficacy was strongly linked to researcher allegiance and this requires further future investigation.



**Contents**



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## 1. Introduction

Obsessive Compulsive Disorder (OCD) is a highly debilitating and disabling illness, associated with significant impairment both of the quality of life of the affected individual and on a wider societal scale in terms of loss of productivity and functioning (Hollander et al. [1]). OCD is relatively common with a 12-month prevalence of approximately 1.2% (DSM-5) [2]. The illness usually emerges in childhood or early adulthood and runs a chronic, relapsing course (Fineberg et al. [3]). Detection of OCD frequently occurs late and many patients experience untreated illness for a significant length of time before receiving treatment (Dell'Osso et al. [4]). Increasingly, evidence suggests that a longer duration of untreated illness leads to poorer outcomes and prognosis (Fineberg et al.) [5]. Therefore, it is of paramount importance that patients with OCD receive appropriate treatment in a timely manner to reduce suffering and improve functioning.

Recommended treatments for OCD include psychological therapy with cognitive behavioural therapy (CBT) involving exposure and response prevention (ERP) (ERP is a therapy in which patients are taught to confront and tolerate conditions that provoke obsessions and compulsions and resist acting on them) or pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI) or the serotonergic tricyclic clomipramine. As SSRI in OCD shows a positive dose-response relationship [6] the highest available dosages are recommended [7].The influential 2005 NICE guidelines (CG31) [8], which were based on a meta-analysis of existing trial data, advocate the use of low intensity psychological treatments (including ERP) for adult patients with mild symptoms of OCD. Monotherapy with either more intensive CBT (including ERP) or an SSRI is recommended for patients with moderate symptoms or patients with mild illness who cannot tolerate low-intensity psychological treatment, whereas combination therapy (SSRI and CBT with ERP) is recommended for patients with more severe or resistant illness. In the case of children and young people with OCD, CBT is prioritised over pharmacotherapy, to avoid potential adverse effects of medication in this age group and ERP is cited as the recommended type of CBT [8]. However, as the original analyses upon which this guidance is based is now more than 15 years old and as more data has since accrued (NICE have stated support for a review of the OCD treatment guidelines) [8,9], it is timely to review the evidence supporting the effectiveness of CBT involving ERP across the age range in OCD.

A large number of individual studies, varying in quality and size, have demonstrated that ERP can be an effective treatment for OCD. These were reviewed in detail in the American Psychiatric Association practice guidelines [7] which also concluded that CBT primarily based on behavioural techniques such as ERP has the strongest evidence base for efficacy. In contrast, the more recently updated British Association of Psychopharmacology guidance cites evidence for ERP monotherapy, cognitive therapy as a monotherapy and a combination of the two as being effective [10]. Indeed, both documents acknowledge that, based on the available evidence, we cannot yet determine which elements of CBT are most responsible for its success. What is, however, clear is that determining the precise type of CBT delivered from reading the descriptions given in many of the published treatment trials can be difficult. It is also evident from the variability within published studies and subsequent meta-analyses (see below) that models and standards vary. Of note, a recent small study in adults (Fineberg et al. [11]) that compared Sertraline monotherapy, CBT with ERP monotherapy delivered strictly according to a manualised protocol, and combination (Sertraline and CBT with ERP) therapy, found disappointing results for CBT with ERP. Whereas combination therapy was the most efficacious treatment option at 16 weeks, the advantage was not sustained and sertraline monotherapy was both the most efficacious and cost effective option at the 52 week endpoint.

Previous meta-analytic evidence has largely focused on CBT rather than specifically on CBT with the ERP. For example, a recent meta-analysis of pediatric OCD by Uhre et al. [12], analysed 12 randomised controlled trials comparing CBT to wait-list, psychological placebo or pill placebo. Although symptoms (as measured by change in CY-BOCS) were significantly reduced by CBT (MD: -8.51, 95% CI: −10.82 to −6.18), all trials included in the analyses were deemed to be at high risk of bias and the certainty of evidence was graded as 'low' or 'very low'. It is important to note that some authors challenged the findings on methodological grounds [13], generating a debate in the journal's pages [14,15]. A network meta-analysis of CBT and pharmacotherapy for adults with OCD by Skapinakis et al. [16,17] was unable to find a clear advantage of one form of treatment over the other. The study identified that most of the patients within the studies who were allocated to CBT were also taking pharmacological treatment, suggesting that these were in fact trials of combination treatment, and further highlighting difficulties in interpreting the results from studies of CBT in OCD (Skapinakis et al. [18]).

Existing meta-analyses have rarely exclusively focused on ERP studies, with most analysing ERP in sub-group analyses of multiple interventions. The earliest ERP for OCD meta-analytic finding often cited is that by Christensen et al. [19] who reported a large effect size (2.34), but this was derived from a pre-post analysis of just one trial. Almost a

decade later Abramowitz (1996) [20] meta-analysed a substantial corpus of 24 trials (29 samples) assessing the impact of ERP on OCD in adults and reported a large effect size of 1.16 for pre-post changes. Pre-post effect sizes however are likely to provide unreliable and inflated effect size estimations because of their lack of a control comparison (see Cuijpers et al. [21]). It is also notable that most studies in this meta-analysis (17/29) had very small samples, with fewer than 10 participants, which is also likely to produce less reliable findings. A second meta-analysis by Abramowitz [22] one year later did examine randomised controlled trials in adult patient samples for whom OCD was the primary diagnosis. The analysis included eight comparisons between versions of ERP and other psychological interventions. The study reported a large effect (using Cohen's d) favouring ERP when relaxation was used as a psychological control treatment ($d = 1.18$; 2 studies), whereas when ERP was compared to cognitive therapy ($d = -0.19$; 4 studies) or individual components of ERP (i.e. response prevention or exposure only) no significant effect of ERP was found ($d = 0.59$; 2 studies). All 8 studies except one used self-report outcome measures and involved in total only 137 participants who received ERP and 105 controls. Around the same time Kobak et al. [23] also reported a large effect size for ERP (0.99 [0.89 to 1.08]) across 36 studies; however this analysis pooled data from within (pre-post) changes and end-point between group changes. Later, another pre-post meta-analysis by Eddy et al. [24] also reported a large effect size of 1.53 for ERP in 16 studies. As noted, such analyses inflate effect sizes and a further analysis was conducted comparing ERP with controls, but this included just 2 trials and indicated an effect size of 1.16.

In a meta-analysis involving both experimental and quasi-experimental designs, Rosa-Alcázar et al. [25] reported a large pooled effect size for ERP in 13 samples (1.127, 0.80 to 1.45) and this was not significantly larger than for cognitive restructuring (CR) alone (1.09) or ERP plus CR (0.998).

Turning to more recent meta-analyses with some component of ERP assessed in children, McGuire et al. [26] meta-analysed 8 randomised controlled trials of individually-delivered ERP tested in children only. In comparisons with non-active controls conditions (mostly waiting-list and relaxation therapy), they reported a large effect size ($g = 1.52$), although this was no larger than for trials using cognitive therapy (1.41). Öst et al. [27] assessed CY-BOCS changes in pediatric OCD both for individual and for group formats of ERP. The effect size for ERP ($g = 0.68$ (95% CI 0.18–1.18, $k = 8$) was somewhat smaller than that of McGuire et al. [26] and smaller than that for Cognitive Therapy ($g = 1.04$ (95% CI 0.45–1.63, $k = 4$) with the effect size for ERP + CT being even smaller and non-significant ($g = 0.35$ (95% CI −0.04 to 0.73, $k = 18$). Öst et al. [28] also published a meta-analysis of adult trials and showed that ERP did not differ in efficacy from CBT at reducing Y-BOCS scores at end-of-trial (0.07 [95%CI -0.15 to 0.30], $k = 7$) or at follow-up (0.07 [95%CI -0.27 to 0.41; $k = 4$).

Olatunji et al. [29] combined trials of CBT and ERP in both adults ($k = 13$) and children ($k = 3$), and in an assessment of 12 ERP trials, reported a large effect size of 1.35 (CI: 0.96–1.74). However, like McGuire et al. [26], their analysis excluded trials using an active psychological control and the majority (10/12) of control arms comprised wait-list controls. The use of wait-list groups in psychotherapy trials is also associated with exaggerated effect sizes (Furukawa et al. [30]), and it is reasonable to interpret the efficacy of CBT in such studies with caution. Intriguingly, Olatunji et al. [29] were also unable to demonstrate any effect on outcomes of candidate moderators such as age at onset of symptoms, duration of illness, gender, number of CBT sessions or the presence of co-morbidities. However, they did find that the control group moderated the effect size, with wait-list control comparisons revealing larger effect sizes than comparison to placebo controls.

In summary, data from individual randomised controlled trials and existing meta-analyses suggest that CBT with ERP is an effective treatment modality for OCD. Concerns about methodological rigor are however repeatedly highlighted as a limitation on interpreting the available data. In particular, the limitations of previous meta-analyses relate to the assessment of pre-post effect sizes (Abramowitz [20]; Eddy et al. [24]; Christensen et al. [19]) or mixing pre-post and end of trial effect sizes (Kobak et al. [23]); the inclusion of small RCTs (e.g. studies by Abramowitz et al. [22] were mostly <10 per arm); the exclusion of active controls and a focus largely on comparisons with wait-list controls (Olatjunji et al. [29]; McGuire et al. [26]); a reliance on self-report measures (Abramowitz et al. [22]); meta-analysing small numbers of ERP studies (McGuire et al. [26], $k = 8$; Eddy et al. [24] $k = 2$; Abramowitz et al. [22] $k = 8$; Öst et al. [28] $k = 7$; Öst et al. [27], $k = 8$; Christensen et al. [19] $k = 1$), which limits the possibility of examining moderator variables (see Borenstein et al. [31]); the inclusion of non-experimental designs (e.g. Jónsson, H., & Hougaard, 2008; Rosa-Alcázar et al. [25]). Some have examined only children (McGuire et al. [26]; Öst et al. [27]), while others only adults (Abramowitz 1996 [20]; Öst et al. [28]). Most have failed to address publication bias and earlier meta-analyses produced effect size estimates based on fixed effects models. Few existing meta-analyses have assessed study quality (e.g. Öst et al. [28] used a bespoke measure and then examined this in a limited way rather than as a moderator) and none appear to have used a standardised measure risk of bias. It is also notable that, where moderators have been analysed, previous meta-analyses have also found it difficult to confidently identify treatment or patient factors that predict a better outcome with ERP (Hezel and Simpson, 2019 [32]). Moreover, as the focus of previous meta-analyses has been primarily on CBT of any form, rather than one that specifically incorporates ERP, little clarity exists about the superiority of CBT with ERP over other forms of CBT for OCD across the full age range affected. Thus, while CBT with ERP remains the suggested psychological treatment of choice for OCD [6], uncertainty exists regarding its relative efficacy, the methodological quality and coverage of previous meta-analyses as well as the extent to which patient or treatment-related factors might render CBT with ERP the most suitable option for a particular individual.

## 2. Aims

This meta-analysis aims to comprehensively evaluate the available evidence from randomised controlled trials addressing the efficacy of CBT with ERP as a treatment for adults and children with OCD. Therefore, the analysis only includes studies of CBT that incorporate ERP. We also aim to identify whether treatment-related or patient-related factors impact on the treatment-response, in order to aid clinical decision-making. As concerns about the methodological quality of CBT studies have been raised in previous reviews (Olantunji et al. [29], Skapinakis et al. [16]), we aim to conduct a 'risk of bias' quality assessment. As it is evident that the CBT delivered in previous studies has shown considerable variability in quality, we also incorporate an assessment of the fidelity of the CBT with ERP delivered within this meta-analysis. In addition, we assess studies for the presence of researcher allegiance (RA), defined as the researchers' "belief in the superiority of a treatment and in the superior validity of the theory of change that is associated with the treatment" (Leykin & DeRubeis, 2009) [33].

## 3. Method

This meta-analysis was pre-registered with the International Prospective Register of Systematic Reviews (PROSPERO: registration number CRD42019122311) as a systematic review and meta-analysis of cognitive behavioural therapy for OCD. We subsequently refined our search criteria to focus exclusively on those published studies that included an ERP component within the CBT arm, as this is the form of CBT usually recommended for OCD [7,8]. We conducted a systematic search of the literature in accordance with PRISMA guidelines (Moher et al.) [34]. The electronic databases PubMed, PsychINFO and EMBASE were searched for eligible studies. We also checked the reference lists of relevant studies and previous systematic reviews for unidentified

studies and searched for registered trials on www.ClinicalTrials.gov and Google Scholar (http://scholar.google.dk). There was no lower limit with regards to publication date and searches continued until April 2020.

An inclusive search strategy was performed using the terms: 'Cognitive behavioural therapy' OR 'CBT' OR 'exposure response prevention' OR 'ERP' AND 'obsessive compulsive disorder' OR 'OCD' generated 2265 articles. The articles were then screened using the following inclusion criteria:

1. Randomised controlled trials in patients with OCD involving CBT with ERP in at least one treatment arm and a control group (which could be an alternative (non -ERP) psychological treatment, psychological placebo, pharmacological treatment or wait-list).
2. The study employed the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (or similar symptom severity scale) as an outcome measure.
3. Full text article published in English.

Abstracts were initially screened for relevance by two study authors (JR and NF). Papers not meeting these criteria were excluded from the analysis. Accepted studies were then independently assessed by two members of the team (JR and MV) to evaluate whether they incorporated ERP into their treatment. Protocol- disagreements were resolved by discussion and the involvement of a third assessor (NF). A consensus was reached in all cases.

Our inclusive search strategy located a large number of studies, which on closer examination were deemed unsuitable as they did not have a non-ERP comparator treatment arm within their study design. These studies were subsequently extracted and excluded from the analysis. Our aim was to include studies where ERP was fundamental to the CBT being applied. On analysing the studies, it was apparent that significant variability emerged in the level of description of the included ERP components. Therefore, where a published report stated that ERP was an integral component of the CBT being delivered, we included it within our analysis.

### 3.1. Primary outcome

Our primary outcome measure was end-of-trial OCD symptom scores in the CBT with ERP group versus the control group.

### 3.2. Secondary outcomes

#### 3.2.1. Sub-groups

Sub-group analyses were performed on the studies stratified on the basis of type of control: Three of the authors (JR, NF and MV) collaboratively categorised all studies according to the type of control: active psychological treatment (e.g. cognitive therapy, EMDR), psychological placebo (e.g. stress management training), pharmacological treatment (e.g. SSRI), wait-list or treatment as usual (TAU). There were no studies that relied on a pill placebo control. Studies were also grouped and analysed according to whether the study population comprised adults or children.

#### 3.2.2. Moderators

Potential treatment moderators were examined including patient-related factors (age, duration of illness, OCD severity at baseline, depression scores at baseline and end-point) and study-related factors (duration of treatment, control group type, details of control treatment within each arm, experience level of therapists delivering CBT, and information about concurrent medication),

### 3.3. Bias

Each study was assessed for risk of bias using the Cochrane risk of bias tool version 2.0 (RoB2: Higgina Higgins et al. [35]) by two authors (JR and MV) and any discrepancies resolved by discussion. The RoB2 assesses bias that may arise across five domains: bias from randomisation, deviations from intended interventions, missing outcome data, outcome measurement and bias in selection of the reported results.

### 3.4. Exploratory outcomes

Exploratory outcomes, which emerged during the stage of data collection and were therefore not preregistered at PROSPERO, included analysis of the moderating effect of treatment fidelity and the presence of researcher allegiance on effect size.

#### 3.4.1. Treatment fidelity

Based on the descriptions given within each study, an assessment of treatment fidelity was made by an independent CBT expert (LD). This involved assessing each of the components of ERP deemed to be essential e.g. the presence of response prevention, the exposure being prolonged, graded and regular, the therapy being collaborative and the level of experience of the therapist. Each component was given a score of between zero (insufficient information was available to make a decision) and five (awarded where the component appeared was at a level consistent with recognised 'best practice') with a maximum available score of 35 (Individual scores are included in Table 1).

#### 3.4.2. Researcher allegiance

Researcher allegiance was assessed for all trials utilising the 'researcher allegiance assessment tool' used by Turner et al. [36]; adapted from Cuijpers et al. [37]) in a recent meta-analysis that examined psychological interventions in psychosis. Following Turner et al. (2014) [36], we posed the following questions to evaluate the presence of researcher allegiance: Is only one of the interventions mentioned in the title? In the introduction is one of the interventions explicitly described as being the main experimental intervention? Was one intervention specifically described as a control condition? Is there an explicit hypothesis that one treatment is expected to be more effective than the other? If the answer to any of these questions was yes, the study was deemed at risk of researcher allegiance.

### 3.5. Analysis

Data were initially extracted independently by two of the authors (JR and NF), and were then independently re-extracted by another author (KL), with differences being resolved.

Pooled effect sizes were calculated using Comprehensive Meta-analysis, version 3. The effect size employed was Hedges *g*, which is the standardised difference between means, corrected for the tendency towards overestimation in small studies (Hedges, 1981). Effect sizes were calculated comparing end-of trial total Y-BOCS (or alternative scale) scores for the intervention and control groups. Random-effects models were used in all analyses.

Heterogeneity was examined by use of *Q* and $I^2$ statistics. An $I^2$ value of 0–40% suggests that heterogeneity may not be important, 30–60% may represent moderate heterogeneity, 50–90% may represent substantial heterogeneity, and 75–100% may represent considerable heterogeneity (see Higgins & Green, Cochrane Handbook, 2011 [38]). Publication bias was examined using the statistical techniques of Duval and Tweedie's (2000) [39] trim and fill, which aims to estimate the number of missing studies within an analysis and the effect that those studies might have on outcomes.

## 4. Results

Following our search strategy as outlined above, thirty-six trials [11], [40-74 were included in the final analysis Fig. 1.

The trials involved 2020 participants (1005 receiving CBT with a substantive ERP component, and 1015 assigned to a control condition). The comparator control conditions were active psychological treatment ($k = 8$), psychological placebo ($k = 10$), a pharmacological treatment

**Table 1**
Characteristics of studies included in meta-analysis.

| Study | Control arm | Sample number | Age (years) | Females (%) | Therapy Time | Duration of illness | Baseline YBOCS | Concurrent medication allowed | CBT grading |
|---|---|---|---|---|---|---|---|---|---|
| Van Oppen et al. 1995 | cognitive therapy | 57 | 34.7 | 53 | 720 | 13.07 | 24.8 | no | 23 |
| Lindsay et al. 1997 | anxiety management | 18 | 11 | 67 | 900 | 10.95 | 26.57 | yes | 25 |
| Freeston et al. 1997 | wait-list | 29 | 35.8 | 45 | 2430 | 9.4 | 23.5 | yes | 34 |
| de Haan et al. 1998 | clomipramine | 22 | 13.7 | 50 | no info | 0.9 | 22.5 | no info | 29 |
| Van Balkom et al. 1998 | Cognitive therapy | 38 | 33.8 | 45 | 720 | 11.3 | 25.0 | No | 24 |
| McLean et al. 2001 | cognitive therapy | 76 | 35 | no info | 1800 | no info | 21.84 | yes | 33 |
| Cottraux et al. 2001 | cognitive therapy | 65 | 35.8 | 74.6 | 1200 | 13.48 | 28.5 | yes | 8 |
| Greist et al. 2002 | Systematic Relaxation Therapy | 122 (*218) | 39 | 42 | 660 | 22 | 25 | yes | 27 |
| Volpato Cordioli et al. | wait-list | 47 | 36.5 | 51 | 1440 | 21.1 | 25.7 | yes | 6 |
| POTS et al. 2004 | sertraline | 56 (*112) | 11.7 | 50 | 840 | no info | 24.8 | no | 26 |
| Barrett et al. 2004 | wait-list | 48 (*77) | 11.25 | 42.5 | 1260 | no info | 23.3 | yes | 21 |
| O'Connor et al. 2005 | inference-based approach | 32 (*54) | 38.3 | 64 | no info | no info | 22.3 | no | 27 |
| Whittal et al. 2005 | cognitive behavioural therapy (without ERP) | 71 | 35 | not provided | 720 | 13 | 22.5 | yes | 11 |
| Nakatani et al. 2005 | autogenic training | 18 (*28) | 34 | 66.8 | 540 | 12.9 | 30.2 | no | 28 |
| Asbahr et al. 2005 | Sertraline | 40 | 13.7 | 25 | 1080 | 4.8 | 26.3 | No | 27 |
| Foa et al. 2005 | clomipramine | 65 (*122) | 34.9 | 55.4 | 1800 | 16.9 | 25.5 | no info | 26 |
| Sousa et al. 2006 | Sertraline | 56 | 38.5 | 77 | 1440 | 23.5 | 25.1 | No | 25 |
| Anderson et al. 2007 | wait-list | 38 (*61) | 33.2 | 64.3 | 600 | 12.4 | 24 | Yes | 28 |
| Belloch et al. 2008 | cognitive therapy | 29 | 32 | 6.1 | 1800 | 6 | 25.6 | Yes | 11 |
| Freeman et al. 2008 | relaxation therapy | 42 | 7.11 | not provided | 780 | no info | 22.36 | Yes | 23 |
| Khodarahimi et al. 2009 | satiation therapy | 40 (*60) | 24.6 | 0 | 1080 | no info | 37.2 | No | 23 |
| Piacentini et al. 2011 | psychoeducation and relaxation | 71 | 12.3 | 63.4 | 1080 | no info | 24.9 | No | 30 |
| Storch et al. 2011 | wait-list | 31 | 11.1 | 39 | 1080 | no info | 23.4 | yes | 30 |
| Andersson et al. 2012 | attention control supportive therapy | 101 | 34 | 66 | no info | 18 | 21.1 | yes | 24 |
| Belotto-Silva et al. 2012 | fluoxetine | 159 | 34 | 55.1 | 1800 | no info | 25.88 | yes | 21 |
| Visser et al. 2014 | inference-based approach | 90 | 34.8 | 65.7 | 1080 | 15.9 | 26.02 | yes | 21 |
| Herbst et al. 2014 | wait-list | 34 | 35.6 | 65 | no info | 14 | 20.12 | yes | 24 |
| Vogel et al. 2014 | wait-list | 20 (*30) | 34.8 | 65 | no info | no info | 23.8 | no info | 29 |
| Lewin et al. 2014 | treatment as usual | 31 | 5.81 | 29 | 720 | no info | 24.5 | Yes | 22 |
| Mahoney et al. 2014 | treatment as usual | 67 | 39.1 | 59.5 | no info | no info | 33.1 (DOCS scale) | Yes | 20 |
| Freeman et al. 2014 | Family-based relaxation therapy | 127 | 7.2 | 67 | 780 | no info | 25.5 | Yes | 25 |
| Marsden et al. 2016 | eye movement desensitisation reprogramming | 55 | 32 | 61.8 | no info | no info | 25.82 | no info | 28 |
| Fineberg et al. 2018 | sertraline | 31 (*49) | 33.8 | 57 | 960 | no info | 26.8 | Yes | 29 |
| Lenhard et al. 2017 | wait-list | 67 | 14.6 | 46 | no info | no info | 22.5 | Yes | 4 |
| Kyrios et al. 2018 | progressive relaxation training | 179 | 33.4 | 65.7 | no info | 13.7 | 21.94 | yes | 16 |
| Kobayashi et al. 2019 | treatment as usual | 18 | 30.1 | 47.1 | 960 | 10.2 | 27.2 | yes | 16 |

(k = 7), wait-list control (k = 8) and 'treatment-as-usual' (k = 3). All studies used the change in OCD symptom score ratings as the primary outcome; in 35/36 studies this was the Y-BOCS. One study utilised the Dimensional Obsessive-Compulsive Scale (DOCS (Mahoney et al. 2014). Most studies (64%) permitted the use of concurrent psychotropic medication; 25% did not allow concurrent medication and a further 11% did not clearly report this information.

*t*-tests performed showed that intervention and controls did not differ in relation to age, duration of OCD symptoms, baseline Y-BOCS score or depression symptomatology.

The primary analysis demonstrated a large positive effect for CBT with ERP compared to all controls in the reduction of Y-BOCS scores ($g = 0.74$: 95% CI = 0.51 to 0.97). The studies were heterogeneous ($Q(35) = 206.812$, $p < 0.001$) with an $I^2$ value of 83.08. (Fig. 2:.)

### 4.1. Publication bias

Visual inspection of a funnel plot and analysis using Duval and Tweedie's trim and fill method did not suggest the presence of publication bias. (Fig. 3)

### 4.2. Moderator and exploratory analyses

Several moderator analyses were undertaken to evaluate factors that might affect the observed treatment effect size:

### 4.3. Control type

The control groups varied considerably across trials: active treatments as controls (k = 8), psychological placebos (k = 10), pharmacological treatment (k = 7), wait-list (k = 8) and treatment as usual (k = 3). Two out of 7 studies comparing ERP with a pharmacotherapy control involved clomipramine and the rest involved SSRI. Adequate dosages of medication were provided in all but one study (Sousa et al. [56]), in which only a maximum of half the recommended daily dosage of SSRI (Sertraline100mg/day) was provided in the control arm.

Subgroup analyses revealed a significant benefit for CBT with ERP when compared to: psychological placebo (g = 1.13 95% CI 0.71 to 1.55) and wait-list (g = 1.27: 95% CI 0.79 to 1.75). By contrast, trials using active psychological interventions as a control revealed no significant benefit from CBT with ERP (g = −0.05: 95% CI −0.27 to 0.16). In

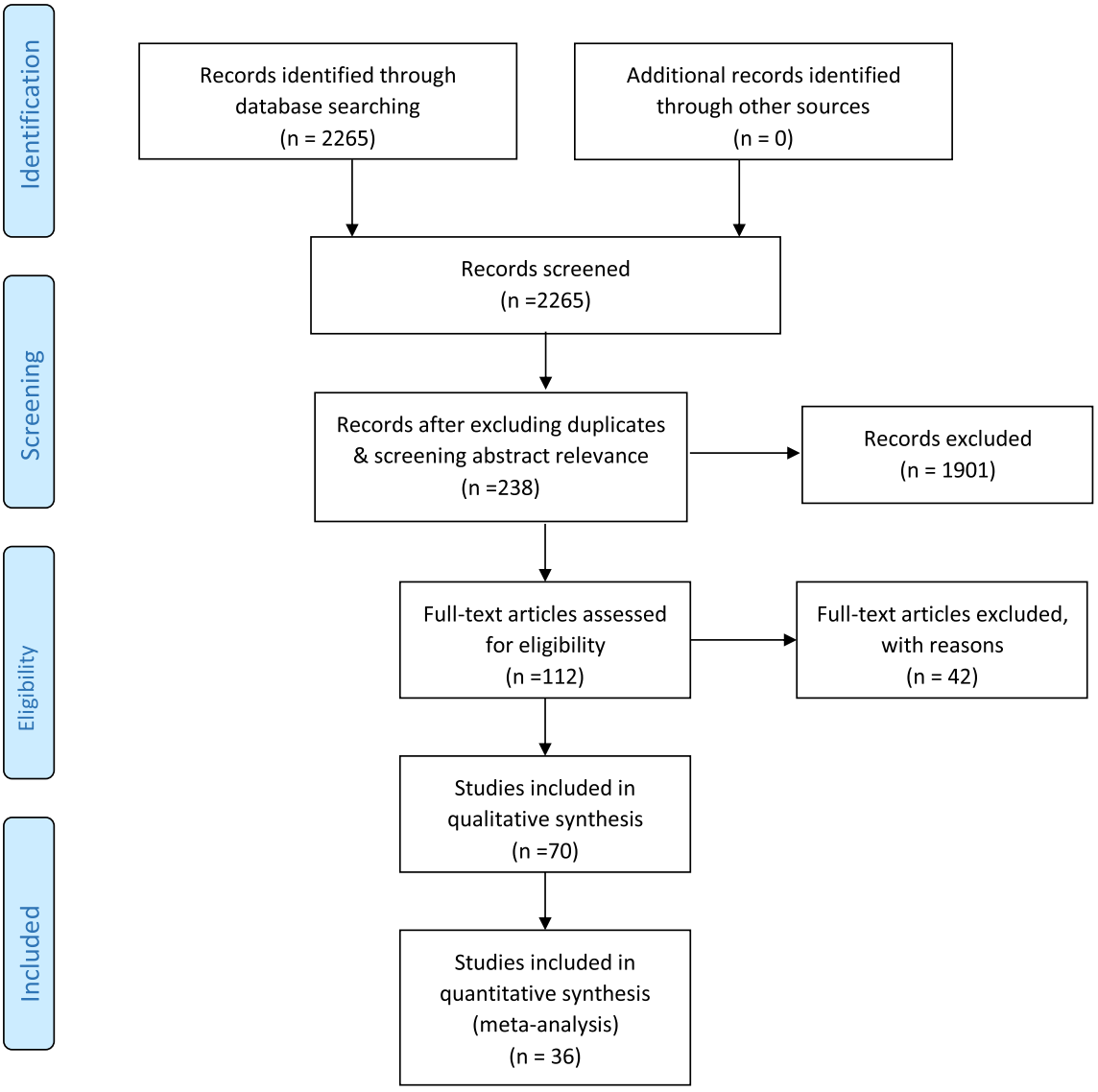


**Fig. 1.** Studies included in systematic analysis.

the case of comparisons with trials of pharmacological treatment, when all pharmacotherapy studies were included, a significant benefit for ERP was seen (g; 0.36: 95% CI 0.07 to 0.64). However, when we excluded the study utilising inadequate dosages of SSRI in the control arm, the effect size when compared to pharmacological controls was only borderline significant ($g = 0.32$: 95% CI -0.00 to 0.64, $p = 0.05$). Treatment as usual trials were not analysed as only three such studies were located. The difference in effect sizes between the groups was significant ($Q = 47.62$, $p < 0.001$).

We calculated the end of trial Y-BOCS mean difference score for CBT with ERP when compared to each intervention type. This was greatest for treatment as usual (10.8: 95% CI: 7.17 to 14.42) and waitlist (8.53: 95% CI: 5.15 to 11.91) and smallest for CBT with ERP compared to active psychological treatment (−0.38: 95% CI: −2.09 to 1.31). In comparison to psychological placebo the mean difference was 5.87 (95% CI: 3.81 to 7.93) and when compared to pharmacological treatment it was 3.15 (95% CI: 0.68 to 5.62).

### 4.4. Researcher allegiance bias

We performed a separate analysis grouping studies according to the presence (k = 28) and absence (k = 8) of suspected researcher allegiance (Fig. 4:). In the studies identified as having researcher allegiance, a very large favourable effect for CBT with ERP emerged ($g = 0.95$: 95% CI 0.69 to 1.2). By contrast, in trials where researcher allegiance was not identified (k = 8), CBT with ERP showed no significant effect on Y-BOCS scores ($g = 0.02$: 95% CI −0.29 to 0.33). The difference in effect sizes between the two groups was significant ($Q = 20.33$ $p < 0.005$).

The mean difference in Y-BOCS score at the end of trial between ERP and controls in for studies with researcher allegiance was 5.99 (95% CI: 4.47 to 7.50) and 0.16 (95% CI: −2.45 to 2.77) for those studies without researcher allegiance.

### 4.5. Adults vs children

Another sub-group analysis was completed to evaluate the effect sizes in studies that were conducted in adult populations (k = 26) versus those involving children (k = 10). The effect size for CBT with ERP was significant both for children (g = 1.09: 95% CI 0.60 to 1.58) and for adults (g = 0.60: 95% CI 0.35 to 0.84). The difference between the two groups was not significant ($Q = 3.14$, $p = 0.08$). The mean difference in Y-BOCS score between ERP and controls at the end of trial was

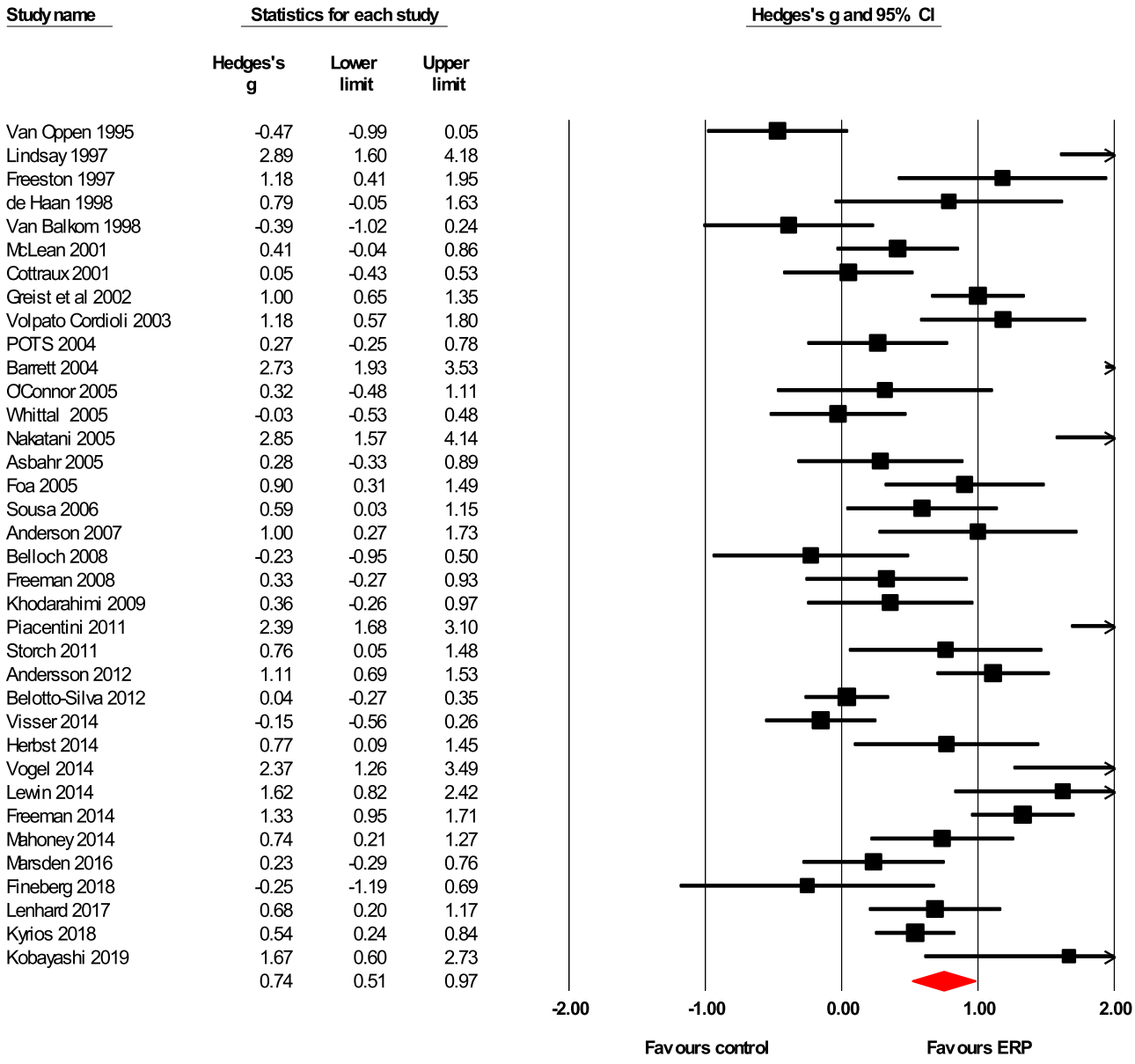


**Fig. 2.** Forest plot showing effect sizes for all included studies.

4.23 (95% CI: 2.42 to 6.03) for adults and 6.51 (95% CI: 3.88 to 9.14) for children.

### 4.6. Group vs individual therapy

A planned analysis comparing trials of group versus individual CBT was not completed due to too few studies (k = 5) employing group CBT.

### 4.7. Other moderator analyses

The impact of age, proportion of females, duration of illness (measured in years), baseline severity (Y-BOCS scores), depression baseline scores on the Beck Depression Inventory (BDI), change in depression scores, total amount of therapy time (measured in minutes) and the fidelity quality of ERP as continuous variables were assessed using meta-regression) Table 2. Only the age of the participant had a significant inverse effect on the effect size.

### 4.8. Risk of bias

On the Cochrane Risk of Bias assessment tool (RoB2) Fig. 5 only 8 studies (22%) were deemed as being at low risk of bias; 14 studies (39%) were assessed as being at high risk of bias and a further 14 (39%) were highlighted as having concerns about bias. In 56% of the studies, potential concerns emerged about the randomisation process, frequently owing to a lack of detail provided in the published trials.

An exploratory analysis (suggested by a reviewer) revealed no significant difference (Q = 0.13, df = 2, $p = 0.94$) in effect sizes for studies rated as at: high risk of bias g = 0.70, 0.53 to 0.98, k = 13, some concern (g = 0.79, 0.50 to 1.08, k = 15) and low risk of bias (g = 0.72, 0.14 to 1.29 k = 8). Despite this, trials at low risk of bias had extremely wide

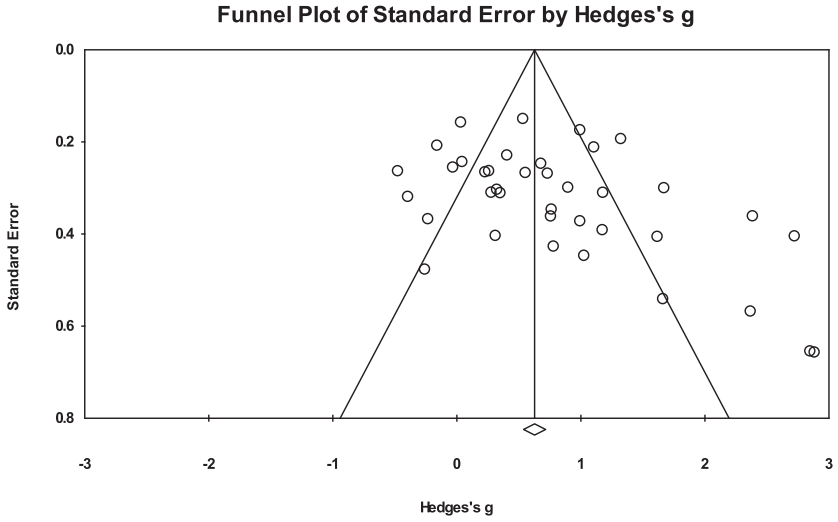


**Fig. 3.** Funnel plot.

**Table 2**
Continuous variables as potential moderators of Y-BOCS effect size at end of trial.

| Co-variate | k | Range | Coefficient | *Z*-Value | *p*-value |
|---|---|---|---|---|---|
| Therapy Time (mins) | k = 27 | 540–2430 | −0.0002 | −0.64 | 0.52 |
| Baseline Y-BOCS score | k = 36 | 19.2–37.2 | 0.0061 | 0.18 | 0.86 |
| Depression baseline score (BDI) | k = 15 | 8.9–24.9 | 0.0415 | 0.85 | 0.40 |
| Duration of OCD symptoms (years) | k = 20 | 0.9–23.5 | 0.0005 | −0.02 | 0.99 |
| Reduction in depressive symptoms | k = 22 | 16.4–78.8 | −0.0078 | −0.96 | 0.34 |
| Female (%) | k = 33 | 0–83.0 | −0.0009 | −0.11 | 0.91 |
| Mean Age | k = 36 | 5.76–39.0 | −0.0272 | −2.73 | 0.006 |
| CBT grading | k = 36 | 4.00–34.0 | 0.0217 | 1.35 | 0.17 |

confidence intervals (0.14 to 1.29), suggesting imprecision and that further low risk trials are required.

## 5. Discussion

This comprehensive meta-analysis, involving 36 RCTs and 2020 participants, evaluates the effectiveness of CBT with ERP in reducing OCD symptoms. Our analysis demonstrated a large pooled effect size for CBT with ERP ($g = 0.74$: 95% CI = 0.51 to 0.97). As far as we are aware, this is the first meta-analysis performed in recent years to focus exclusively on CBT with ERP as the investigational treatment.

Our analyses revealed that the effect size attributed to CBT with ERP depends strongly on the choice of control comparator. Thus, CBT with ERP was more efficacious than psychological placebo (such as psychoeducation, progressive relaxation therapy and autogenic training), with a large pooled effect size ($g = 1.13$ 95% CI 0.71 to 1.55). By contrast, when compared to active psychological treatments such as cognitive therapy or EMDR, the pooled effect size of CBT with ERP was not significant ($g = 0.05$: 95% CI -0.27 to 0.16, $p = 0.62$). Similarly, whereas our analysis found a small advantage for CBT with ERP when compared to pharmacological treatment across all available trials ($g = 0.36$: 95% CI 0.07 to 0.64), the advantage is marginal when adequate dosages of pharmacological treatment are provided in the control arm ($g = 0.32$: 95% CI -0.00 to 0.64, $p = 0.05$).

In terms of interpreting the findings, it is notable that most ERP trials have permitted concurrent medication at stable doses; only 9 (25%) of studies explicitly stated they did not allow concurrent medication (Table 1), meaning that for the majority of studies, a proportion of patients were in reality, receiving combination therapy rather than CBT with ERP as monotherapy. This observation aligns with the findings of Skapinakis et al. (2016 [16]). Although the number of studies utilising clearly defined CBT with ERP monotherapy is small (k = 9), we noted that there were differences between these groups; the participants in the monotherapy studies were younger, had higher baseline Y-BOCS scores and also received less therapy time than in the other studies. Interestingly, the studies of CBT with ERP monotherapy had numerically higher CBT grading scores (Table 1). This could indicate that the monotherapy studies in this meta-analysis had greater CBT fidelity and/or more rigorous reporting of their methodology.

This meta-analysis therefore adds weight to current recommendations regarding the effectiveness of ERP, but does not indicate a significant superiority for ERP compared to other active psychological treatments including some currently posited to be effective for OCD and raises questions about the superiority of ERP over pharmacological treatment for OCD. Consequently, our findings question current clinical guidance (e.g. the 2005 NICE guidelines [8]) prioritising the use of CBT with ERP over other CBT modalities or pharmacological treatment for those with OCD. Indeed, NICE [8] acknowledges that alongside ERP, clinicians working in the field of OCD frequently provide "different variants" of cognitive therapy as well as a combination of cognitive therapy and ERP applied as a "coherent package'.

Furthermore, NICE [8] asserts that whereas "ERP and cognitive therapy have different theoretical underpinnings", as, for example, "most current cognitive therapy explicitly seeks behaviour change but is not operating within a habituation paradigm", it is "uncertain whether either treatment is superior to the other, or indeed whether combining these interventions confers any added benefit (Abramowitz [12]). NICE [8] additionally draws attention to the difficulty of comparing ERP with different variants of CBT owing to a tendency for the treatment modalities to overlap.

Turning to risk of bias, concerns were identified for three-quarters of all published ERP trials (78%), highlighting the need for studies with robust methodology and rigorous reporting. Aside from the far fewer numbers of trials at low risk of bias, they also had very wide confidence intervals, suggesting high imprecision in the effect size estimate and that further low risk trials are required. After 25 years of ERP for OCD trials, currently fewer than 300 participants have received ERP for OCD in existing high quality trials.

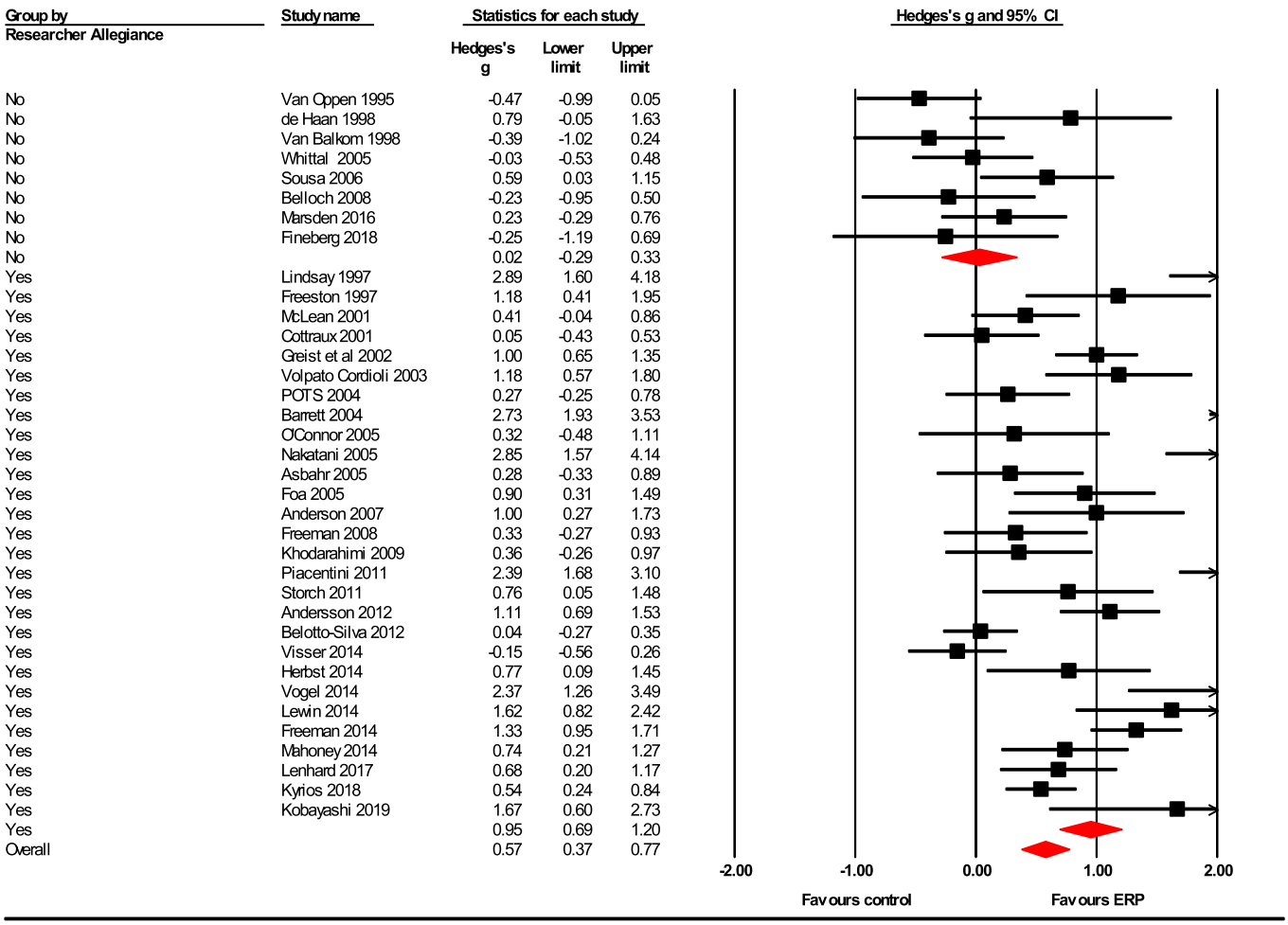


**Fig. 4.** Forest plot for studies grouped by presence of researcher allegiance.

A driver of the overall confidence interval is, of course, the individual trial sample sizes that contribute to the pooled effect. As noted, trials at low risk of bias had the widest confidence intervals, although those for high risk trials were also wide. We note that high risk trials had – on average – 50% fewer participants than low risk trials and are insufficiently powered to detect even the large effect size reported here. By contrast, low risk trials were sufficiently powered to detect the large effect size. Thus, while the wide confidence intervals for high risk trials may reflect underpowering, the wider confidence intervals for low risk trials would not seem to be wholly attributable to the under-powering of trials.

In addition to assessing risk of bias, this is the first study to look at the role of researcher allegiance in studies of CBT with ERP in the treatment of OCD. Our results demonstrate a clear difference in effect size related to our ratings of researcher allegiance. Notably, over three quarters of all trials (28/36: 78%) were classified as showing researcher allegiance and those trials produced a large significant effect size ($g$ = 0.95: 95% CI 0.69 to 1.2). Indeed, all studies that demonstrated a statistically significant beneficial effect for CBT with ERP were assessed as having researcher allegiance. By contrast, in studies not displaying researcher allegiance, the effect of CBT with ERP was nonsignificant ($g$ = 0.02: 95% CI -0.29 to 0.33, p 0.89). The number of trials without researcher allegiance was small (k = 8) and so some caution may be required when interpreting this result. Nevertheless, the finding that 78% of studies included in this meta-analysis were evaluated as being at high risk of researcher allegiance is concerning in itself and highlights this as an area of research that requires further exploration.

Researcher allegiance appears to operate, in part, via study design features favouring not only the preferred treatment, but crucially perhaps the preferred control comparison. In this context, we note that the trials with high and low researcher allegiance differed markedly in terms of the types of control group they employed.[1] While 7/8 (87.5%) low-allegiance trials employed active controls, only 8/28 (28.6%) high allegiance trials had active controls. In fact, *only* high-allegiance trials used TAU or wait list control (wait-list comprising almost 30% of all high-allegiance trials). That wait-list controls can inflate effect sizes in psychotherapy trials is well-known and one possibility is by creating nocebo effects in control groups (Furukawa et al.) [30]. For the corpus of trials examined in the current meta-analysis, the average pre-post change in Y-BOCS scores for wait-list arms was just 3.3%, compared with 30.9% for all other control comparators combined (and 22.6% after removing 'active' control arms involving CBT). In their discussion of control choice, Leichsenring & Steinert (2017) [75] remarked correctly that "When examining efficacy, a treatment may be compared with different comparators, that is, with an established treatment, treatment as usual, a placebo, or a waiting list, with *decreasing strictness of the empirical test*." (p.1323, our italics). The adoption of a wait-list control condition in psychotherapy trials is not only a possible methodological weakness, but a mechanism that allows researcher allegiance to potentially interfere (Dragioti et al. [76]).

[1] We thank a reviewer for noting this

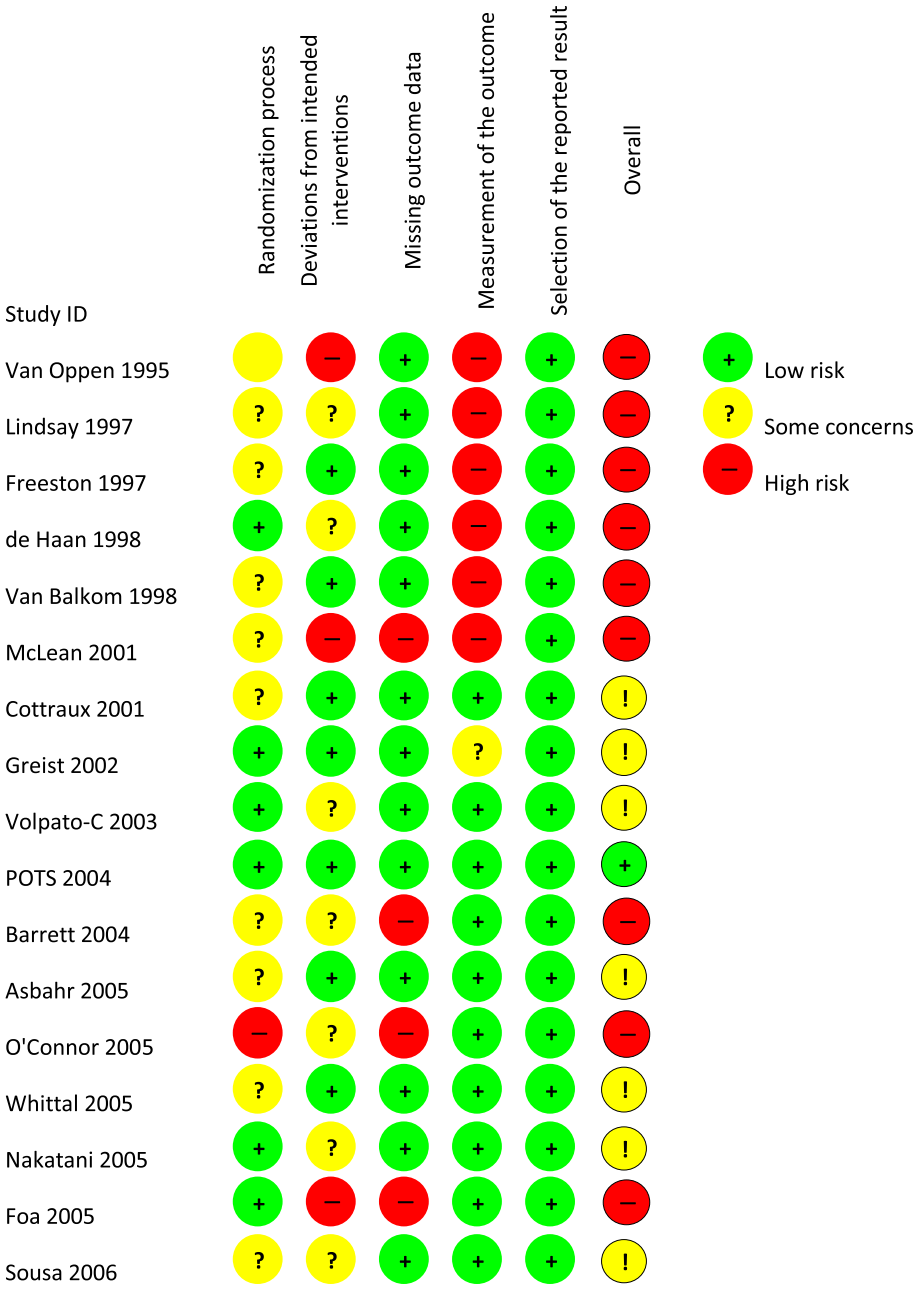


**Fig. 5.** ROB2 assessment.

Moreover, the effects of researcher allegiance persist even after methodological quality is controlled (Munder et al. [77]). Researcher allegiance thus apparently exerts effects beyond designing the study in a way which benefits the preferred treatment. This does not imply nefarious intent of researchers; it may simply reflect that researcher enthusiasm or expertise for a preferred treatment is not fully represented in the variables commonly coded as methodological characteristics. However, one potential clinical implication is that the efficacy of CBT with ERP is dependent upon therapist factors and, importantly, that patients may have an inferior outcome if treated in centres whose expertise does not focus on ERP.

We also evaluated the fidelity of the CBT with ERP within the individual studies. In terms of statistical analysis, we could not demonstrate that the quality of CBT with ERP (as graded by an independent assessor) impacted upon its effectiveness. However, during the process of extracting the data, it was noted that sufficiently detailed information about study design, in particular with regards to the fidelity of the CBT with ERP delivered, was frequently missing. This would be expected to have impacted upon the reliability of the grading in our analysis.

Our findings therefore concur with the conclusions of previous meta-analyses (Öst et al. [28], Skapinakis et al. [16]), which highlighted problems with methodological quality in published studies on CBT for OCD. These inadequacies substantially compromise interpretation of the existing evidence. As a result, caution should be applied when attempting to draw conclusions and guide treatment based on results from such studies. A pressing need exists for high quality studies of CBT with ERP in order to establish clinical utility.

Moderator analyses typically address questions about who might most benefit from an intervention (such as CBT) and how we might improve outcomes for those who benefit least. We found an inverse

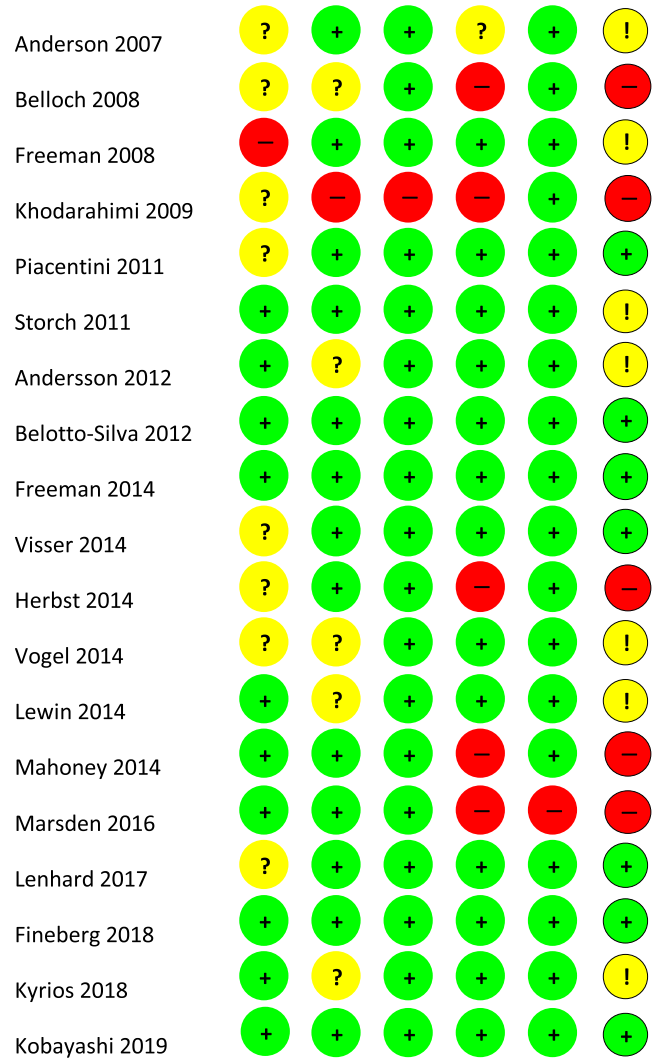


**Fig. 5** (*continued*).

relationship between effect size and age on meta-regression, suggesting ERP may work best in the young. Results from naturalistic longitudinal studies suggest younger patients may respond more favourably to treatment (Mancebo et al. 2014) [78]. It is possible that this result however reflects a confound with duration of illness, which was found not to significantly affect the ES in this analysis, but as the sample giving duration of illness data was small this analysis was probably underpowered.

Aside from age, we found a series of null relationships for the moderators examined (therapy time, baseline Y-BOCS severity, baseline depression, reduction of depression symptoms, OCD duration, proportion of female participants, and CBT with ERP fidelity rating). The failure to find significant (sample, treatment, or participant) predictors for efficacy accords with the meta-analytic findings of Olatunji et al. (2013) [29], who also failed to detect any significant impact of plausible moderators on CBT outcomes. Although such findings may appear counter-intuitive, they are consistent with the notion that CBT may be beneficial to most people diagnosed with OCD: As noted by Olatunji et al. (2013) [29], the absence of significant moderators potentially "highlights the effectiveness of CBT for patients with wide range of symptom complexity". (p. 39).

However, variables such as 'baseline severity' and 'amount of treatment delivered' would reasonably be expected to affect the outcome of an efficacious treatment. We therefore suggest that the demonstrable lack of methodological rigor and reporting could also explain why, as of yet, we lack reliable evidence to indicate which patient and treatment factors might predict response and thus guide clinical decision-making. It is possible that other study and patient characteristics have a moderating effect, but as yet remain unstudied. For example, 'adherence to homework tasks' has previously been demonstrated to be a significant predictor of treatment outcome (Simpson et al. [79]) but is not consistently reported in studies.

A change of 5 Y-BOCS points is known to represent a clinically meaningful change in clinical status (Hollander [1]. We may therefore interpret the mean between-intervention difference in the end-of-trial Y-BOCS scores as an additional crude estimate of the 'clinical importance' of the reported effect sizes. (This metric assumes the comparator groups had equivalent scores at baseline.) Using 5 Y-BOCS points as a benchmark, it can be seen that CBT with ERP produced clinically important advantages compared to treatment as usual, waitlist and psychological placebo. In contrast, there was no clinically important advantage for ERP over other active forms of psychological treatment and the advantage over pharmacological treatment was indeterminate. Furthermore, based on Y-BOCS differences, the effect of ERP appeared clinically important only in those studies where researcher allegiance was present and appeared more robust in studies of children than adults.

Finally, discrepancies emerge between the large effect size demonstrated for CBT with ERP in this analysis (which is supported by the effect sizes seen in previous analyses) and the more modest effects observed in naturalistic clinical practice, in which setting a sizeable proportion of patients fail to achieve benefit (Eisen et al. [80]). This could potentially be due to the existence of moderating variables which, to date, remain unidentified. Uncovering such moderators may enable us to predict for which patients and in which conditions CBT with ERP is likely to be most effective. Future studies of CBT with ERP should be designed with sufficient statistical power to enable the identification of such moderators.

## 6. Conclusions

Having subjected all the published randomised controlled trials of CBT with ERP for OCD to meta-analysis, we find this intervention appears to be effective. However, when the studies were parsed according to the choice of comparator control, no advantage for CBT with ERP was found in those studies where an active psychological treatment was used as the control comparator. This casts doubt on the superiority of CBT with ERP over other forms of psychological therapy for OCD. Whereas CBT with ERP was significantly superior to pharmacological treatment when all eligible studies were analysed, the effect became marginal and only approached significance when adequate pharmacotherapy dosages were used in the control arm. Our meta-analysis further highlights concerns about the methodological rigor and reporting of published studies of CBT with ERP in OCD, with only a minority of studies deemed to be at low risk of bias. In addition, an exploratory analysis revealed that the positive effect for CBT with ERP was restricted to those studies showing evidence of researcher allegiance in favour of CBT with ERP, questioning its generalizability. This finding highlights the need for further research into the presence and implications of researcher allegiance within studies of psychological therapy in OCD. In sum, an unmet need remains for rigorously designed randomised controlled trials to investigate the patient and treatment related factors governing the efficacy of CBT with ERP for OCD.

## Declaration of Competing Interest

Prof. Naomi A. Fineberg declares that in the past 3 years she has held research or networking grants from the ECNP, UK NIHR, EU H2020, MRC, University of Hertfordshire; she has accepted travel and/or hospitality expenses from the BAP, ECNP, RCPsych, CINP, International Forum of Mood and Anxiety Disorders, World Psychiatric Association, Indian

Association for Biological Psychiatry, Sun; she has received payment from Taylor and Francis and Elsevier for editorial duties. In the past 3 years, she has accepted a paid speaking engagement in a webinar sponsored by Abbott. Previously, she has accepted paid speaking engagements in various industry supported symposia and has recruited patients for various industry-sponsored studies in the field of OCD treatment. She leads an NHS treatment service for OCD. She holds Board membership for various registered charities linked to OCD. She gives expert advice on psychopharmacology to the UK MHRA.

Dr. Jemma Reid, Prof. Keith Laws, Dr. Matteo Vismara and Dr. Benedetta Grancini report no financial relationships with commercial interests.

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