A Systematic Review and Meta-Analysis on the Effectiveness of Exposure and Response Prevention Therapy in the Treatment of Obsessive-Compulsive Disorder.

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Abstract

Exposure and Response Prevention (ERP) is considered the most effective psychotherapeutic treatment for Obsessive-Compulsive Disorder (OCD). The literature supports its adoption yet results vary and vagueness regarding therapy protocol exists. We present an updated review and meta-analysis to provide clarity in the comparison of strict ERP protocol to control or active therapy groups. Moderator analyses were conducted to investigate treatment effect of cognitive elements, hours of therapy and duration of OCD.

A systematic literature search, concluded in January 2021, identified twenty-four studies, published between 1997 and 2018, including a total of 1,134 patients. The main analysis assessed the difference between pre-treatment and post-treatment scores compared amongst ERP and the other groups.

We found a statistically significant different reduction in pre-treatment to post-treatment Yale-Brown Obsessive Compulsive Scale scores between ERP therapy versus other groups. We also found a statistically significant moderation effect of cognitive elements. The other two moderators, hours of therapy and OCD duration, were non-significant.

Our review suggests that ERP was superior to the other groups, including both neutral and active treatments, in reducing OCD symptomatology and should therefore be recommended as an optimal therapy. Future research should focus on tailoring ERP to the individual and investigating further refinements.

Keywords: Obsessive-Compulsive Disorder, Exposure with Response Prevention, Meta-analysis.

Introduction

Background

Obsessive-Compulsive Disorder is frequently considered to refer to an exaggerated preoccupation with perfectionism and cleanliness, which is often even encouraged (Durna et al., 2019). Albeit rates of sub-clinical obsessive and compulsive tendencies are seen in the general population (Stein, 2002), these traits do not capture the reality of living the disorder. Clinical OCD is rather common, with a lifetime prevalence of around 2% (Mayerovitch et al., 2003; Ruscio et al., 2010), presenting an often chronic and debilitating progression. Patients experience unwanted obsessions, compulsions or both – respectively defined as: persistent thoughts, urges or impulses that cause anxiety or distress and repetitive behaviours performed in response to an obsession or rigid rules (American Psychiatric Association, 2013). Avoidance, the physical evasion of triggering stimuli, also considerably impacts sufferers (McKay et al., 2015). Although all those with clinical diagnoses will experience these major symptoms, OCD is heterogeneous in nature; various sub-types of the disorder will reflect the individual's personal idiosyncratic worries (Robbins et al., 2019). These generally centre around specific themes: harm, accompanied by checking compulsions; symmetry, accompanied by ordering rituals; contamination, accompanied by washing routines; sex, violence and religion, accompanied by mental rituals, and also seen in the other sub-types (McKay et al., 2004; Abramowitz et al., 2010). These symptoms are highly time-consuming, distressing and detrimental to daily life, leading to impairments in global Quality of Life (QoL) outcomes (Coluccia et al., 2016), thereby differing from subclinical presentations. Finally, OCD is often comorbid with other psychiatric disorders, such as Generalised Anxiety Disorder and Major Depressive Disorder (MDD) (Nestadt et al., 2001; Brakoulias et al., 2017).

Once thought to be intractable, with available psychoanalytic therapies generally ineffective, OCD is now considered to be manageable thanks to a multitude of psychotherapeutic and pharmacological treatment alternatives (Abramowitz, 1998; Foa, 2010; Foa and McLean, 2016). Cognitive-Behavioural Therapy (CBT) based on Exposure with Response Prevention (ERP) is widely considered the go-to treatment with the most empirical support (Abramowitz, 2006b; Abramowitz and Arch, 2014) capable of significantly reducing obsessive, compulsive, depressive and anxious symptoms (Abramowitz, 1996; Olatunji et al., 2013; McKay et al., 2015; Öst et al., 2015). Generally, ERP-based psychotherapy is more or

equally as effective as Selective Serotonergic Reuptake Inhibitors and clomipramine, the pharmacotherapies of choice for OCD (Kobak et al., 1998; Sousa et al., 2006; Skapinakis et al., 2016). A combination of the two therapies, especially for severe cases, is also a recommended course (Kobak et al., 1998; Eddy et al., 2004; Romanelli et al., 2014). Further, ERP manifests advantages in terms of relapse; 12% compared with clomipramine 45-89% (Simpson et al., 2004; Abramowitz et al., 2009). Other types of psychotherapy, such as Cognitive Therapy (CT) also lead to treatment gains (Fisher et al., 2020). Comparisons of psychological therapies, though, have provided mixed results: some studies finding that ERP is more effective (Abramowitz et al., 2002; Fisher and Wells, 2005; Ponniah et al., 2013) and others that it is as effective (Gava et al., 2007; Rosaalcazar et al., 2008; Skapinakis et al., 2016) as other interventions. Moreover, these findings are additionally ambiguous as ERP and CT delivery in the clinic greatly overlaps and the differences between them are often undiscernible (Abramowitz, 1998; Gava et al., 2007; McMillan and Lee, 2010).

Despite the breadth and efficacy data of treatment options, treatment remains a pertinent issue for patients with OCD and clinicians alike. For the former, concerns including stigma, embarrassment and loss of control often lead to treatment deferral (Newth and Rachman, 2001) – many avoid seeking treatment altogether (Mayerovitch et al., 2003; Torres et al., 2007), or delay between 9 and 17 years (Ruscio et al., 2010; García-Soriano et al., 2014). Complete remission and treatment adherence are also concerns; patient relapse or treatment discontinuation rates range between 12% and 50% (Simpson et al., 2004; Abramowitz and Arch, 2014). Continuation of research to maximise therapeutic potential is necessary. To do so, we must turn to the pathological models underlying the disorder, and subsequent examination of treatment delivery.

Pathological models of OCD

The functional relationship between obsessions and compulsions can be elucidated from a behavioural learning perspective. Originating from Mowrer's two-factor theory of anxiety disorders (Mowrer, 1956, 1960), it posits that classical conditioning evokes acquisition of fear towards a previously neutral stimulus. The fear association is subsequently maintained by operant conditioning via avoidance or performance of compulsions. Insofar as compulsions are performed to momentarily reduce fear and anxiety brought by obsessions, they become

negatively reinforced and repeated, creating a vicious cycle and preventing extinction learning of the conditioned fearful response (Abramowitz, 2006a).

Cognitive theories illustrate the mechanisms behind the attribution of fear and anxiety. Foa and Kozak (1985) first suggested that erroneous cognitions were driving OCD behaviour. Salkovskis (1985) proposes that, as a result, obsessions become problematic due to their role as stimuli themselves in inciting negative automatic thoughts, or intrusions, idiosyncratic to the individual's personal belief system. Thus, intrusive thoughts become pathological by virtue of the salience attributed to them through erroneous cognitions. These include: 1) thinking something is the same as acting upon it; 2) failing to prevent harm is the same as causing harm; 3) inflated responsibility; 4) failure to perform compulsions is the same as wanting harm to occur; and 5) needing to control one's thoughts. Finally, research shows that certain beliefs relate to specific symptoms, such as 'perfectionism' with checking and 'needing to control ones thoughts' with washing (Taylor et al., 2010).

The two theories come together to form the cognitive-behavioural model, which is the most extensively supported (Abramowitz et al., 2009). Dysfunctional cognitive beliefs lead to salience of intrusive thoughts thereby causing anxiety and distress which become conditioned. In seeking to reduce the discomfort via ritualising or avoiding triggers, these coping mechanisms become negatively reinforced and prevent the opportunity to learn that the stimuli is neutral. Further, both obsessions and compulsions act as triggers, perpetuating the broken system.

ERP in practice

ERP therapy developed from Meyer's (1966) ground-breaking approach which incorporated previous behaviour research (Abramowitz, 2006a) based on prolonged exposure to distressing stimuli to modify "patients expectations". Today, therapy is guided by a widely used and comprehensive treatment manual (Foa et al., 2012), developed via evidence-based research supporting necessity of: *in vivo* and *imaginal* exercises (Foa and Goldstein, 1978; Foa et al., 1980); combined exposure with response prevention (Foa et al., 1984); daily up to weekly sessions (Abramowitz et al., 2003a; Foa et al., 2012); and therapist guidance (Abramowitz, 1996; Tolin et al., 2007).

Together, the therapist and patient construct a hierarchy of *in vivo* and *imaginal* exposure exercises designed to evoke patient-specific anxiety and distress. The former involves physical interaction with 'fearful' stimuli (leaving objects in the 'wrong' place or touching something 'contaminated'). *Imaginal* exposure consists of mental engagement with situations that are difficult to be exposed to in real life. Exposures are initially conducted in-session and subsequently assigned as homework. The therapist may also perform home visits. Following exposures, patients are encouraged to refrain from acting upon the compulsions that succeed the exercises, known as ritual prevention. A discussion then ensues regarding the feelings experienced during exposure, providing an opportunity for the patient to learn interactively. Due to the highly distressing nature of the therapy, prior to its commencement the patient is informed about the purpose of the exercises during a 'psychoeduction' session, instrumental in maintaining the patient's motivation (Abramowitz, 2006a). Relapse prevention is also tackled once the hierarchy has been completed. This helps patients fully understand their progress, make a list of learnt strategies and prepare them for the possibility of relapse. Overall, the manual envisions between 17 and 20 sessions lasting from 90 to 120 minutes, carried out weekly up to daily.

The mechanisms of change include a behavioural aspect – extinction learning of the conditioned fear response – combined with a cognitive element – where patients dysfunctional beliefs are disconfirmed – and a self-efficacy factor – where patients master their fears by not relying on avoidance or rituals (Abramowitz, 2006a). Yet there are competing theories as to how this occurs. Emotional Processing Theory (EPT) (Foa and Kozak, 1986; Foa and McNally, 1996), posits that during ERP a competing, more easily retrievable, non-pathological fear structure is created. The theory emphasizes that within-session and between-session *habituation* of the fear response, or decreased anxiety, is a marker of success. Critiques of EPT highlight that *habituation* is not always a predictor of treatment outcome or learning (Craske et al., 2008; Kircanski et al., 2012), and could encourage patients to think anxiety is a negative state rather than a normal behaviour (Jacoby and Abramowitz, 2016). These authors instead propose an inhibitory learning approach (Abramowitz and Arch, 2014), whereby fear *tolerance* and the acceptance of intrusive thoughts is favoured over *habituation*. This model emphasizes the role of expectancy violation, focused on disproving immediate expectations around experiencing obsessional thoughts, uncertainty about fears, anxiety around stimulus confrontation and ability to tolerate negative states associated with exposure at a higher intensity and length (Jacoby and Abramowitz, 2016). Exposure exercises are designed to

violate said expectations, although cognitive restructuring still occurs indirectly as a consequence (Abramowitz, Taylor and McKay, 2005).

Rationale

We have elucidated the pathological models that underly OCD and how ERP tackles the behavioural relationship between obsessions and compulsions to alleviate symptoms. We have also seen how OCD is underscored by a substantial cognitive component, which upholds the comprehensive pathological model of the disorder, the adoption of ERP-based CBT treatments or pure CT. The significant overlap in CBT and CT and the often obscured integration of cognitive elements in what is reported as ERP, has led to confusion regarding treatment protocol in the review literature on psychotherapy for OCD (Abramowitz, 1998; Gava et al., 2007; McMillan and Lee, 2010). Indeed, cognitive techniques targeting dysfunctional beliefs are regularly integrated into ERP, which is often called just CBT (Öst et al., 2015). Previous meta-analyses comparing such treatments, as discussed above, have shown mixed results and have not compared specific interventions with pharmacotherapies but have compared all psychological, all pharmacological or both therapies separately (Fisher and Wells, 2005; Gava et al., 2007; Rosaalcazar et al., 2008; Skapinakis et al., 2016). Further, the issue of overlapping treatments during comparison, instigating further research into specific intervention effects, has been called upon (Knopp et al., 2013; Ponniah et al., 2013). This was one of the primary motivations for the current investigation, prompting an updated literature review and meta-analysis of ERP treatment with very strict criteria. This would ensure a highly targeted investigation to elucidate effectiveness of a specified treatment.

We also sought to build on previous meta-analyses via various means. Firstly, we would only consider studies that followed the ERP protocol outlined above. Protocols assessing ERP as a booster to another therapy or ERP with added elements such as family-based or mindfulness-based ERP, were all excluded. Further, we would not consider studies assessing self-help ERP, internet-based ERP or intensive ERP protocols such as the Bergen-4-Day-Treatment. It was important to include studies that maintained sufficient therapist-patient contact since research has been inconclusive in determining the number of hours needed for treatment effect and, importantly, the therapist holds an essential role during treatment, particularly in maintaining motivation (Tolin et al., 2007; Pearcy et al., 2016). Previous reviews have included studies with a variety of ERP protocols and included ERP designs with limited therapist contact or exposure as homework only in one analysis (Ponniah et al., 2013; Fisher et al., 2020).

We focused solely on studies adopting the Yale-Brown Obsessive-Compulsive Scale (YBOCS) as the main outcome measure; it is widely considered to be the 'gold-standard' for measuring OCD symptoms (Abramowitz, 2006a) and has excellent validity (Kim et al., 1990; Woody et al., 1995). Further, various meta-analyses on the topic have used multiple outcome measures (Abramowitz, 1996; Eddy et al., 2004; Gava et al., 2007; Rosaalcazar et al., 2008), which could lead to standardization bias (Morris and Deshon, 2002; Öst et al., 2015). In view of the YBOC's strong reliability and validity and the statistical discrepancies that arise from combining outcome measures, adoption of the YBOCS as the single outcome measure was preferable.

We included self-reported YBOCS, which has been shown to be as reliable and consistent as the clinician-reported scale (Federici et al., 2010), while others excluded (Öst et al., 2015).

We only included studies conducted with patients over 18 years-of-age, whereas other reviews had mixed adults and children trials (Kobak et al., 1998; Gava et al., 2007; Olatunji et al., 2013; Romanelli et al., 2014). Adult (late-onset) and paediatric (early-onset) OCD have been found to differ significantly and to represent distinct etiological sub-types of the disorder, thus inclusion of both could moderate treatment evaluation results (Geller et al., 1998; Mancebo et al., 2008; Taylor, 2011).

We included studies involving patients with comorbidities, who have been shown to respond equally well to treatment, in order to be representative of the OCD population (Franklin et al., 2000; Brakoulias et al., 2017).

Next, we conducted a pre-treatment to post-treatment efficacy comparison, as we wanted to compare within-subjects symptom reduction depending on group allocation. This design provides an advantage to others, such as post-test only, where evaluation occurs only after the treatment (Morris, 2008).

We also wanted to address the lack of clarity regarding the inclusion of cognitive elements in the ERP procedure (Abramowitz, 1998; Abramowitz et al., 2002; Abramowitz and Houts, 2005; McMillan and Lee, 2010). This could lead to differences in the way that therapists between trials deliver the therapy, potentially generating varying treatment effects. Hence, we conducted a further analysis to investigate whether the adjunct of cognitive elements would have a moderating effect on treatment effectiveness. Other moderators of interest that could influence practice and efficiency of treatment were hours of therapy and duration of OCD. The

former served to demonstrate whether fewer hours are as effective as a higher amount, which is significant for clinical practice. Moreover, previous reviews have reported conflicting results regarding the role of this moderator (Abramowitz et al., 2002; Rosaalcazar et al., 2008). Next, assessment of treatment effectiveness depending on the number of years spent with the disorder is another noteworthy investigation due to patient's lengthy treatment deferral. Furthermore, the relationship between duration of OCD and treatment outcome is very complex (Dell'Osso et al., 2009), with some studies having found it predicts outcome (Eisen et al., 2013), and others that it does not (Steketee and Shapiro, 1995), thus warranting further research.

Our review and meta-analysis consisted of an extensive literature search, after which our pre-defined criteria were applied to identify studies for inclusion. We deemed twenty-four studies fit to be explored in the meta-analysis, where our main investigation compared the reduction between pre-treatment and post-treatment in YBOCS scores for ERP treatment, versus absence of intervention or other psychotherapeutic or pharmacological therapies.

Methods

Protocol

"Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) protocol was adopted for methodology and reporting (Liberati et al., 2009; Moher et al., 2009). Specific objectives and methods for this research were delineated prior to its commencement.

See *Figure 1* for the PRISMA Flow diagram.

Inclusion and exclusion criteria

Exclusively Randomized Controlled Trials (RCT) were included, with the following additional criteria for *inclusion*. Studies accepting subjects over 18 years of age and with a primary diagnosis of OCD as defined in either the International Classification of Disorders (ICD) (World Health Organization, 2018) or the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013). Studies that included patients with comorbid disorders were also considered as long as the primary diagnosis was OCD. Trials assessing ERP as the main intervention, compared with placebo, waiting-list or other active interventions with pre-treatment and post-treatment YBOCS scores as the primary outcome (Castro-Rodrigues et al., 2018). Either interview or self-report YBOCS scales were accepted as both are comparatively reliable and consistent (Federici et al., 2010). Both individual or group therapy studies were included as per their demonstrated equivalence (Pozza

and Dèttore, 2017; Öst et al., 2015). Treatment had to include both exposure and response prevention elements (Foa et al., 1980). Finally, remote ERP treatment was considered provided there was ongoing patient-therapist contact equivalent to a non-internet-based therapy, and all essential steps of ERP were covered.

Criteria for *exclusion* were as follows. Observational, case studies or reports, case control and cohort or studies assessing children or adolescents were not considered. Trials lacking a detailed account of treatment protocol, or employing limited treatment therapist coaching or self-controlled exposure were also excluded. ERP assessed in conjunction or as a booster to another therapy or with any additional elements, were considered to have invalid control groups. We could not include studies that compared ERP alone versus ERP with added elements as then any statistical effect would be due to the added elements and not ERP. Lastly, we excluded studies lacking sufficient data such as lack of individual pre-treatment and post-treatment YBOCS scores and Standard Deviations (SD), as per our statistical design.

There were no limitations as to number of participants, population, severity of OCD symptoms or OCD domain (sub-type).

Information sources

The following electronic databases were used for the study search: PubMed, Google Scholar and Science Direct. An additional study search was conducted by manually examining individual studies and past meta-analyses and systematic reviews on the topic. All articles available in English were included.

Search

An initial electronic search was conducted using a defined and limited search in June 2019. The search was limited to studies published since 1971, when the first RCT on ERP therapy occurred (Rachman et al., 1971). An advanced PubMed search was carried out, using the keywords *OCD*, *ERP* and *randomized* and excluding the keyword *paediatric*, resulting in 42 articles. A Science Direct search was conducted using the keywords *OCD*, *ERP*, *randomized*, resulting in 739 articles. Finally, an advanced Google Scholar search was conducted using the keywords *OCD*, *ERP* and *RCT* and excluding the keyword *paediatric*, resulting in 990 articles. The total number of articles acquired from the database

search was 1,771. An additional manual investigation provided a further 121 articles. An updated search was carried out in January 2021, following the same procedure but limited to the years 2019-2021. The PubMed, Science Direct and Google Scholar searches resulted in 11, 163 and 231 articles respectively and 3 articles were found manually, totalling 408.

Study selection

The 1,892 articles found during the initial search, and the 408 articles found in the updated search, were scanned for duplicates, leaving 2,226 articles to be screened for basic acceptability. The titles and abstracts were inspected for eligibility criteria and a total of 144 articles were subsequently read in full and evaluated for adherence to inclusion and exclusion criteria. 120 articles were excluded for the following reasons: not RCT, invalid control group, not on ERP, invalid ERP protocol, insufficient therapist coaching, no YBOCS, follow-up, not OCD, included 18's, missing data, not original data. 24 studies met all of the criteria and were included in the final analysis.

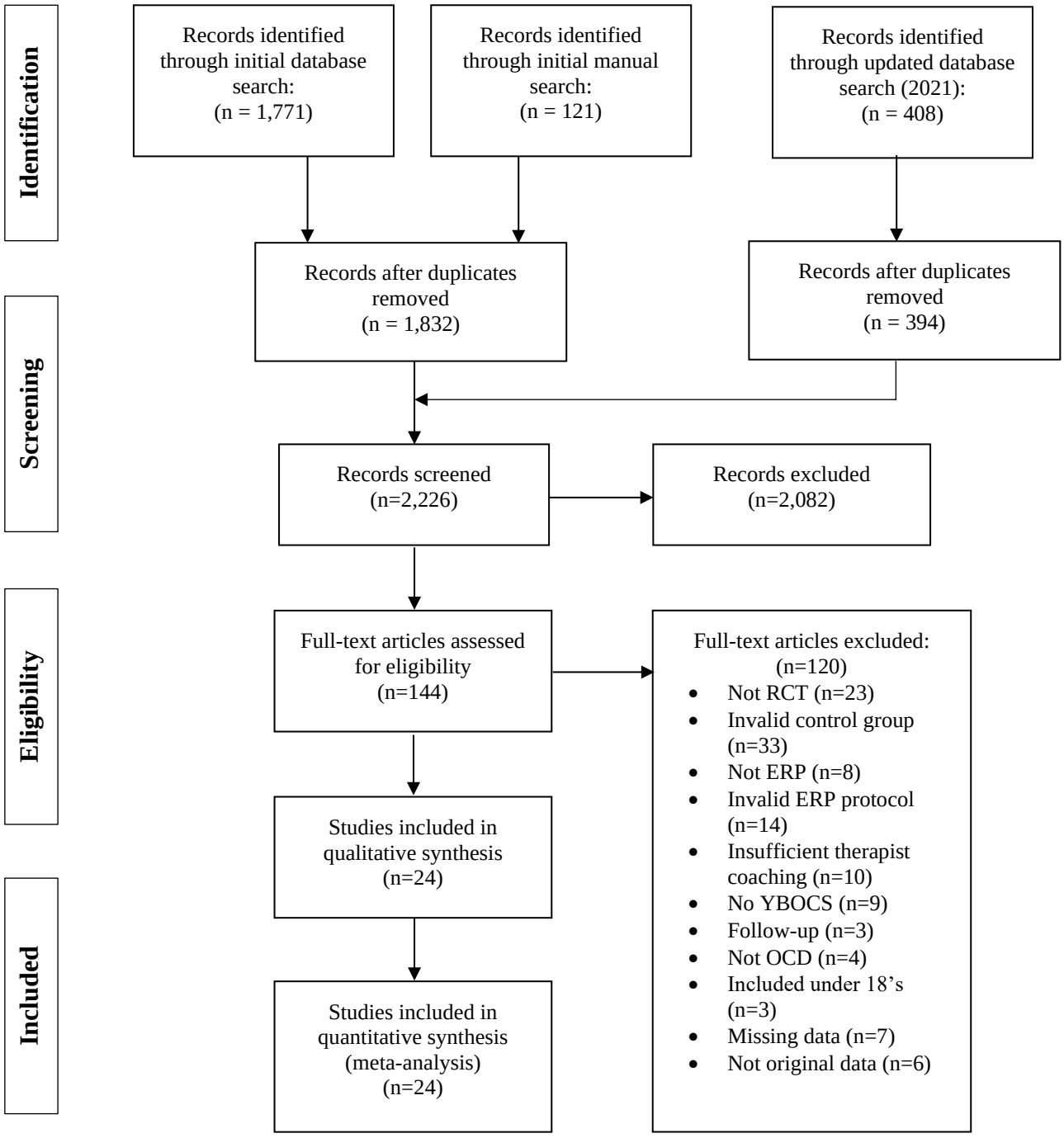


Figure 1: Adapted PRISMA Flow Diagram showing the procedure followed for study selection into meta-analysis according to PRISMA guidelines (Moher et al., 2009). 24 studies met all the criteria and were included in the final meta-analysis.

Data collection

Data was manually extracted from the published articles. Where possible, data from treatment completers was used; alternatively, information from the intent-to-treat population was entered. See *Table 1* for basic patient demographics and study information.

Where data was not available, authors were contacted to request its provision, particularly with regards to the inclusion of cognitive elements in the ERP procedure. Where no information was attainable, Not Applicable (NA) was noted. In two cases (Gomes et al., 2016; Visser et al., 2015) SDs were extrapolated from other data following Cochrane guidance for systematic reviews and meta-analyses (Higgins and Green, 2011). See Appendix 1 for the data extrapolation process.

Study	Type of Therapy		N		% Female		Age (SD)		OCD duration (SD)	Total therapy (hours)	Cognitive element	YBOCS report	Minimum (YBOCS) score for inclusion	OCD sub-type	Country
Author	ERP	C/OT	ERP	C/OT	ERP	C/OT	ERP	C/OT	ERP	ERP	ERP	Interview/ self-report	all	all	
Lindsay et al., 1997	ERP	AM	9	9	44	89	31.6 (8.9)	34 (9.3)	9 (8.7)	15	N	Interview	NA	NA	Australia
Freeston et al., 1997	ERP	WL	15	14	NA	NA	NA	NA	NA	40.5	Y	Interview	NA	Obsessions only	France
O'Connor et al., 1999	CBT	WL	6	6	33	50	33 (6.7)	41.5 (16)	10.4 (3.9)	22	Y	Interview	NA	NA	Canada
Cottraux et al., 2001	ERP	CT	32	30	66	83	34.8 (11.4)	36.8 (9.8)	11.4 (8.7)	20	NA	Interview	≥16	NA	France
McLean et al., 2001	Group ERP	Group CT	32	31	NA	NA	NA	NA	NA	30	N	Interview	NA	Washing/cleaning, Checking, Harm, Sexual and miscellaneous (Ordering, Hoarding, Counting, Repeating, Mental Rituals)	Canada
Cordioli et al., 2003	Group CBT	WL	23	24	NA	NA	NA	NA	NA	24	Y	Interview	≥16	NA	Brazil
Simpson et al., 2004	ERP	PP	18	2	50	100	33.1 (10.5)	33.5 (12)	13.6 (12.2)	36	NA	Interview	≥16	NA	USA
Vogel et al., 2004	CBT	WL	16	12	56	42	31.4 (10.4)	37.8 (13.2)	NA	24	Y	Interview	NA	Washing/cleaning, Checking, Covert rituals, Hoarding	Norway
O'Connor et al., 2005	ERP	IBA	12	16	NA	NA	NA	NA	NA	NA	N	Interview	NA	NA	Canada
Foa et al., 2005	ERP	PP	29	26	62	38	33.8 (8.9)	34.3 (11.4)	14.4 (11.5)	36	Y	Interview	≥16	NA	USA
Nakatani et al., 2005	ERP	AT	10	8	70	62	32.5 (11.2)	35.9 (8.7)	10 (7.1)	9	NA	Interview	>16	Aggression, Contamination, Sex, Hoarding, Religion, Symmetry, Miscellaneous, Somatic	Japan
Fineberg et al., 2005	Group CBT	Group RT	24	17	75	76	37.5 (11.1)	41.4 (13)	NA	24	Y	Interview	≥16	NA	UK
Whittal et al., 2005	ERP	CBT	29	30	52	73	34.2 (11.3)	35.6 (9.7)	11.1 (9.9)	11	N	Interview	NA	NA	Canada

Sousa et al., 2006	Group CBT	Sertraline	25	25	NA	NA	NA	NA	NA	24	Y				
Anderson and Rees, 2007	ERP	WL	17	14	65	64	32.2 (7.6)	34.4 (10.2)	11.4 (9)	12	Y	Interview	NA	NA	Australia
Belloch et al., 2008	ERP	CT	13	16	62	60	34.2 (13)	30.2 (5.7)	6.8 (6.8)	20	N	Interview	NA	Pure obsessions (Aggressive, Sexual, Moral/Religious obsessions); Obsessions with overt compulsive rituals (Checking, Cleaning, Superstition); Both pure obsessions and obsessions with overt compulsive rituals	Spain
Jaurrieta et al., 2008	ERP	WL	19	19	NA	NA	24.2 (6.7)	23.3 (6.6)	NA	15	Y	Interview	>16	Aggressive, Contamination/Cleaning, Doubting/Checking, Sexual, Collecting, Religious, Ordering/Symmetry, Somatic, Repetition, Slowness	Spain
Khodarahimi, 2009	ERP	WL	20	20	0	0	NA	NA	NA	18	NA	Interview	NA	NA	Iran
Belotto-Silva et al., 2012	Group ERP	Fluoxetine	70	88	56	55	33.9 (11.1)	34.1 (10.6)	NA	24	Y	Interview	≥ 16	NA	Brazil
Visser et al., 2015	CBT	IBA	47	43	60	72	33.7 (8.5)	35.9 (10.6)	NA	18	Y	Interview	≥16	NA	Netherlands
Gomes et al., 2016	Group CBT	WL	52	46	58	67	44.5 (14.3)	37.1 (13.3)	30 (13.5)	24	Y	Interview	≥16	NA	Brazil
Challacombe et al., 2017	ERP	TAU	17	17	100	100	32.4 (NA)	32.7 (NA)	NA	12	Y	Interview	NA	NA	UK
Fineberg et al., 2018	CBT	Sertraline	16	15	62	47	NA	NA	NA	16	Y	Interview	> 16	NA	England
Marsden et al., 2018	CBT	EMDR	26	29	65	59	33.3 (15.4)	30.9 (9.8)	NA	16	Y	Self	Not clear	NA	UK

Table 1: all twenty-four included studies and relevant demographic and study information.

C/OT=Control/Other Therapy; AM=Anxiety Management; WL=Waiting-List; CT=Cognitive Treatment; PP=Pill Placebo; IBA=Inference-Based Approach; AT=Autogenic Training; RT=Relaxation Training; TAU=Treatment-As-Usual; EMDR=Eye Movement Desensitisation and Reprocessing; Y=Yes; N=No; NA=No information; SD=Standard Deviation

Risk of bias

Following PRISMA guidelines a risk of bias evaluation was conducted, aimed at highlighting possible methodological and clinical sources of bias (Liberati et al., 2009), ensuring an accurate assessment of intervention effects (Higgins and Green, 2011). We therefore followed Cochrane guidelines to assess sources of potential bias in each study, reported in the Results (Higgins and Green, 2011).

Statistical analysis

Statistical analyses were performed using Rstudio with metafor package for meta-analysis (Viechtbauer, 2010).

Prior to the main analysis, to ensure there were no significant differences between the groups across studies in initial OCD severity, a Standardized Mean Difference analysis between the pre-treatment YBOCS scores was conducted.

The main analyses were conducted following pretest-posttest-control procedure (Morris, 2008). We aimed to assess the difference in intervention effect by comparing within-group changes in pre-treatment and post-treatment scores between groups (ERP and 'other'). This design is advantageous in ensuring regulation of pre-existing differences as each participant acts as their own control (see Morris (2008)). Thus, the primary outcome of difference between treatment and 'other' in YBOCS change was assessed to quantify the impact of the ERP therapy. This consisted of a quantitative within-group and between-group analysis using a linear fixed-effects model within the metafor package (The Metafor Package, 2017). First, the within-group component was calculated; for each study, we obtained the standardized mean change values (yi) and sampling variances (vi) between pre-treatment and post-treatment scores for all groups. The variable specifying the raw correlation coefficients between pre-test and post-test scores (ri) was not obtainable. As per the guidelines (The Metafor Package, 2017), we searched for and selected estimated values based on known properties and long-term test-retest reliability of the YBOCS (Woody et al. 1995). 0.61 was thus selected as a representative estimate for the raw correlation coefficient variable. Next, we conducted a sensitivity analysis to ensure that altering the correlation would not affect the results of the meta-analysis. Hence one value in each direction was selected: 0.71 and 0.51, and the meta-analysis carried out for each. Next, the difference in the standardized mean

changes between the two groups was calculated for each study. Finally, the main meta-analysis was conducted, to achieve an effect size of the reduction in YBOCS depending on allocation.

We then assessed the influence of the selected moderator variables: addition of cognitive elements, number of hours of therapy and years of OCD duration. Variables were separately evaluated as moderators to symptom reduction within a mixed-effects model meta-analysis (Viechtbauer, 2010). First, the standardised mean change between pre-treatment and post-treatment for the treatment group was calculated, using the method previously outlined (Morris, 2008). Next, the cognitive elements moderator, a categorical variable, was coded dichotomously (0 if it included cognitive elements or 1, if it did not). The other two variables, hours of therapy and years of OCD duration, were coded as continuous.

Finally, a heterogeneity of variance assessment was made. For the preliminary and main meta-analysis the Q-statistic was used. This value indicates the similarity in outcome between studies beyond chance, or the variability in intervention effects, which should not be significant (Higgins and Green, 2011). For the moderator variables, we used the I^2 statistic to represent the residual heterogeneity contributing to the unaccounted variability, and the H^2 statistic to indicate the ratio of unaccounted variability to sampling variability.

Results

Risk of bias assessment

Our risk of bias report is summarised in *Table 2*. As per our criteria, all studies randomized participant allocation ensuring a low risk of selection bias in this regard. Only five studies reported on allocation concealment, with three adhering and two not. All studies were assessing an active psychotherapeutic treatment therefore blinding of participants and personnel was not feasible. Blinding of outcome assessment was adhered to by fourteen of the twenty-four studies. Fourteen out of twenty-four studies explained procedures for dealing with incomplete data. Other sources of bias included expectancy bias in Simpson et al. (2004), as patients and clinicians were aware of when the treatment sessions would come to an end; no independent assessor for the outcome measures (Vogel et al., 2004); lack of inter-rater reliability assessments in Foa et al. (2005) and Visser et al. (2015) indicating that the outcome scores were not cross-referenced; baseline differences in group demographics in Fineberg et al. (2005); men-only in Khodarahimi (2009); no protocol integrity checks in

Belotto-Silva et al. (2012); and use of estimates for calculating duration of therapist contact and females only in Fineberg et al. (2018).

	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias
	Random sequence generation	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective reporting**	**Other bias**
Lindsay et al. (1997)	L	U	U	U	U	U	U
Freeston et al. (1997)	L	U	U	U	L	U	U
O'Connor et al. (1999)	L	U	H	L	U	U	U
Cottraux et al. (2001)	L	U	U	U	L	L	U
McLean et al. (2001)	L	U	U	U	L	U	U
Cordioli et al. (2003)	L	L	H	L	L	L	U
Simpson et al. (2004)	L	U	U	L	L	U	Expectancy bias for end of treatment
Vogel et al. (2004)	L	U	L	H	L	U	Did not use an independent rater
O'Connor et al. (2005)	L	U	U	L	U	U	U
Foa et al. (2005)	L	U	L	L	L	U	No inter-rater reliability assessments
Nakatani et al. (2005)	L	U	U	L	U	U	U
Fineberg et al. (2005)	L	U	H	L	L	U	Different group demogra-phics
Whittal et al. (2005)	L	U	U	L	H	U	U
Sousa et al. (2006)	L	U	U	L	U	U	U
Anderson and Rees (2007)	L	U	U	U	L	U	U
Belloch et al. (2008)	L	U	U	L	L	U	U
Jaurrieta et al. (2008)	L	L	H	U	L	U	U
Khodarahimi (2009)	L	U	U	U	U	U	Men only
Belotto-Silva et al. (2012)	L	U	U	L	L	U	No protocol integrity checks

Visser et al. (2015)	L	U	L	L	U	U	No statistics for inter-rater reliability
Gomes et al. (2016)	L	H	H	U	U	U	U
Challacombe et al. (2017)	L	L	L	L	L	U	U
Fineberg et al. (2018)	L	H	H	L	H	U	Assumptions used to calculate contact
Marsden et al. (2018)	L	U	U	Self-assessment	L	L	U

L=low risk; H=high risk; U=uncertain risk.

Table 2: Cochrane risk of bias assessment tool. Each study has been quality assessed for the 6 potential sources of bias and given a code and colour equivalent to the degree of bias. Green sections with 'L' indicate the study has scored a low risk of bias; red sections with 'H' indicate the study has a high risk of bias in this area; and yellow sections with 'U' indicate the study has an uncertain risk of bias on this measure.

Preliminary tests

As a preliminary test we compared pre-treatment YBOCS scores between the treatment and 'other' groups. There was no significant difference in pre-treatment YBOCS scores, with an estimate of 0.03 (95% CI=[-0.09 – 0.15]; SE= 0.06; z= 0.46, p= .644). The test for heterogeneity was not significant, (Q-statistic= 27.41, p= .239), indicating that variation was not attributable to studies being diverse from one-another. Thus, there was no difference between the groups on this measure.

Main analysis

For the main meta-analysis, we conducted a sensitivity exploration by altering the correlation variable (ri). We conducted the analysis using 0.51 (estimate= -0.76; SE= 0.09; z= -8.50; p< .01), 0.61 and 0.71 (estimate= -0.74; SE= 0.08; z= -9.30; p< .01), and consistently achieved the same results; the sensitivity analysis was therefore satisfactory and altering this variable did not impact our findings. Since the true values of ri for each study were not attainable, our sensitivity exploration demonstrates that our results were not impacted and are consistent. Here are reported the results from the test using the 0.61 correlation as was established in the literature (Woody et al. 1995). Our meta-analysis revealed a statistically significant difference between ERP and the 'other' groups in YBOCS score reduction at pre-treatment versus post-treatment. This was indicated by a mean effect size, effect size= -0.75, significant at p<.01 (95% CI= [-0.92- -0.59]; SE= 0.09, z= -8.87). The results can be visualized in *Figure 2*.

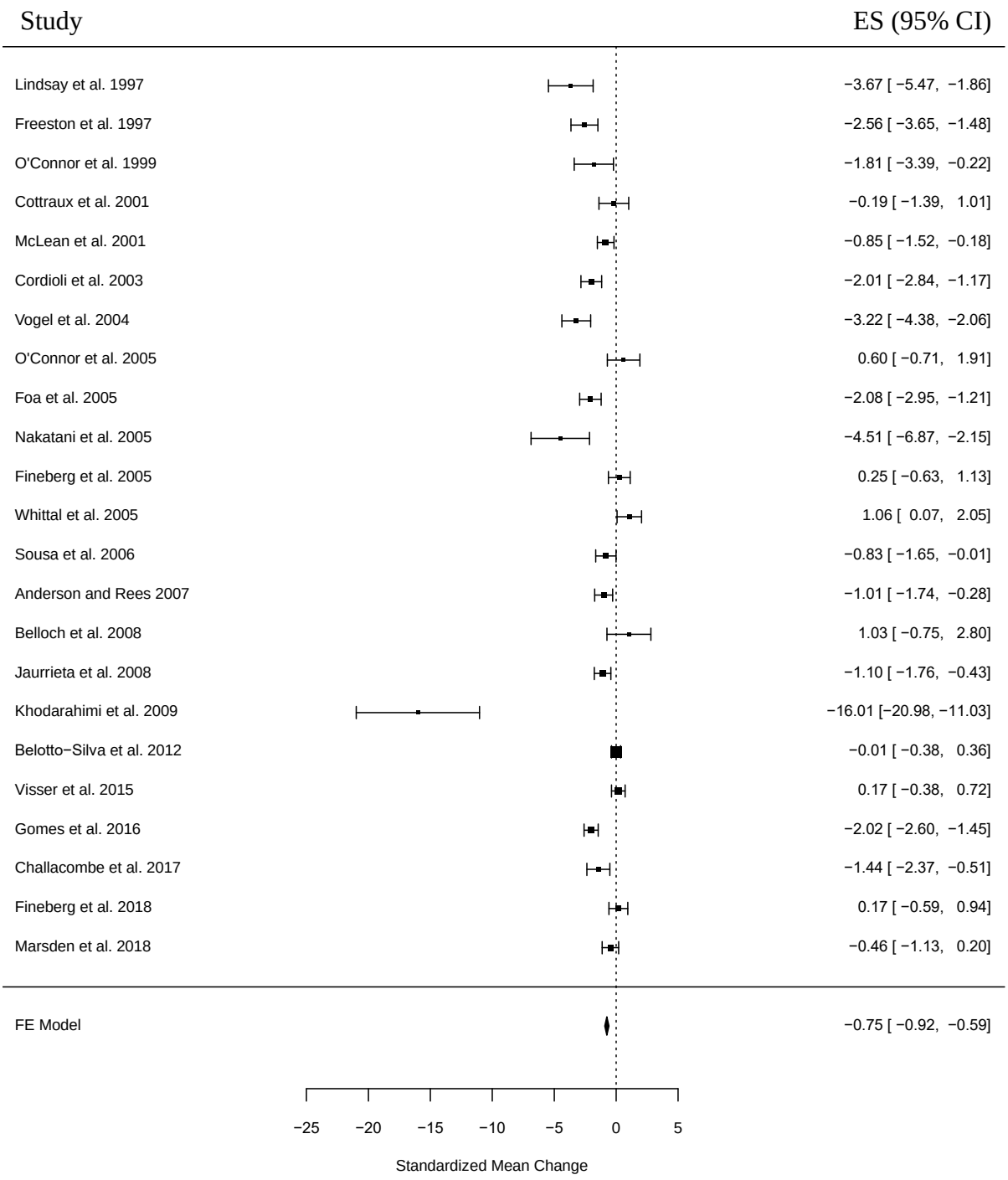


***Figure 2*:** Forest plot displaying the reduction in YBOCS scores from pre-treatment to post-treatment between ERP therapy and 'other' groups for each study included in the meta-analysis. Each row represents a different study, with the authors and year on the left-side column; on the right are the effect size (ES) and CIs; in the middle of the plot, across from each study, is the standardized mean change, with the points on the negative side of zero on the bottom key indicating a significant study result and on the positive side of zero a non-significant study result. Each study also has a different size point, which represents the relative weighting to the overall result. The final row before the bottom key indicates the over fixed-effects model result as stated above.

Our test for heterogeneity was significant (Q-statistic= 185.66, $p< .01$), indicating that one study could be driving the results as there is some unexplained heterogeneity between studies. Cochrane guidelines, used throughout this piece, report that when using a fixed-effects

model the heterogeneity result can be ignored (Higgins and Green, 2011). Regardless, to ensure that any individual study was not driving the heterogeneity, a leave1out test was conducted. This computation runs the main meta-analysis excluding each study successively, therefore assessing whether the results remain significant each time, eventually confirming the reliability of the main analysis (Viechtbauer, 2010). The *p*-values were significant for each test, therefore our main meta-analysis was not affected by the heterogeneity between the studies. Additionally, we ran influential case diagnostics on the studies to identify any outliers and potential influential cases, following guidelines used throughout the statistical analysis (Viechtbauer, 2010). The adopted *influence* function generated eight diagnostic plots (see Appendix 2), to reveal studies 19, 20 and 21 (Belotto-Silva et al., 2012; Visser et al., 2015 and Gomes et al., 2016 respectively) as outliers and potential drivers of the results. This can be deduced from their influence on the fit of the model (Cook.d and hat plot) and large residuals (rstudent plot), whereby their removal would reduce the amount of residual heterogeneity (Tau2.del). Thus, we ran the meta-analysis without studies 19, 20 and 21 to assess whether our analysis would still yield significant results, which was the case (effect size= -0.97, significant at $p<.01$ (95% CI= [-1.18- -0.76]; SE= 0.11, z= -8.94)). This, combined with the leave1out test, demonstrates that our original results can be considered valid.

Moderator analyses

The first moderator analysis examined whether the addition of cognitive elements within treatment would affect the significant reduction in pre-treatment to post-treatment YBOCS scores after ERP therapy. The test of moderators was significant (QM= 160.04; $p<$ .001). Although, both treatment with (estimate= -1.74; 95% CI= [-2.13 - -1.35]; SE= 0.20; z= -8.68, $p<$ .001) and without (estimate= -2.87; 95% CI= [-3.48 - -2.26]; SE= 0.31; z= -9.20, $p<$ .001) cognitive elements lead to a significant reduction in YBOCS scores at pre-treatment versus post-treatment. This suggests both treatment variations significantly reduce OCD symptoms. The test of heterogeneity was significant (QE= 113.24; $p<$ .001). The residual heterogeneity that was contributing to the unaccounted variability was, I^2= 82%, and the ratio of unaccounted variability to sampling variability was, H^2= 5.54. These results can be disregarded as we had already conducted additional heterogeneity tests for the main meta-analysis and the results remained unaffected.

Next, we assessed whether number of hours of therapy affected the reduction in YBOCS pre-treatment to post-treatment. The moderator effect of hours of therapy was not

significant, QM= 1.46, at *p*= .227, indicating that number of hours did not predict treatment outcome. The output confirmed that there was a significant difference between pre-treatment and post-treatment in general, indicated by the intercept being significant, (estimate= -1.49; 95% CI= [-2.57 - -0.42]; SE= 0.55; *z*= -2.72, *p*< .05), thus confirming the results of the main meta-analysis. Although the moderator effect was not significant (estimate= -0.03; 95% CI= [-0.08 – 0.02]; SE= 0.03; *z*= -1.21; *p*= .227), indicating that number of hours did not alter the reduction in YBOCS between pre-treatment and post-treatment. Again, the test of heterogeneity was significant (QE= 128.68; *p*< .001; I^2= 85%; H^2= 6.87), although we can discount it once again.

The final moderator analysis assessed the impact of years of OCD duration on pre-treatment to post-treatment score change. The moderator was not significant, (QM= 0.11; *p*= .738), indicating that years living with the disorder did not affect pre-treatment to post-treatment score. Accordingly, the effect of the duration variable was non-significant (estimate= 0.02; 95% CI= [-0.08 – 0.12]; SE= 0.05; *z*= 0.33, *p*= .738). Again, we obtained significant heterogeneity (QE= 38.76; *p*< .001; I^2= 79%; H^2= 4.76), although we can discount it.

Discussion

Results summary

Our main aim was to determine whether ERP-based therapy was more effective in reducing OCD symptoms compared to no treatment or other psychotherapeutic or pharmaceutical interventions. Our strict study selection with particular attention to treatment protocol allowed us to determine results with a high degree of accuracy and specificity. In such manner preventing other confounding variables, both in treatment – such as self-controlled exposure, mindfulness-based CBT or self-help programs – and in-review methodology – such as concomitant inclusion of adults and children, from influencing the results. By building upon past meta-analyses and a multitude of trials, we attempted to highlight valuable insights for clinicians and their patients.

Ultimately, we included twenty-four RCTs carried out in 11 countries, published between 1997 and 2018 and concerning a total of 1,134 patients in our analysis. The efficacy of ERP therapy in reducing OCD symptoms was compared to a control group, either waiting-list or placebo, or another therapy, which included anxiety management, cognitive therapy, IBA, autogenic training, relaxation therapy, fluoxetine, sertraline and eye-movement

desensitisation and reprocessing. Our meta-analysis showed that there was a greater reduction in pre-treatment to post-treatment OCD symptoms, as measured via the YBOCS, for patients that received ERP than for any of the 'other' groups. Thus, ERP was more efficacious than no treatment or other available alternatives included in the meta-analysis. Additionally, we can confirm that our results were not impacted by pre-existing differences in OCD severity, measured in the pre-treatment scores. This finding coincides with past investigations (Abramowitz, 1996; Fisher and Wells, 2005; Olatunji et al., 2013; Ponniah et al., 2013; McKay et al., 2015; Öst et al., 2015), and thus new trials have added to the pool of significant ERP treatment outcome for OCD.

We subsequently performed additional analyses, to investigate the role of specific moderator variables as predictors of ERP success. As has been discussed throughout, whether the 'standard' ERP procedure contains cognitive elements is unclear (Abramowitz and Houts, 2005), and this could lead to differences in the effectiveness and patient response to ERP. One of our aims was to clarify its effect. Treatments both with and without cognitive elements resulted in statistically significant changes in pre-treatment to post-treatment YBOCS scores. This was unexpected due to the ample support for the cognitive-behavioural theory of OCD (Abramowitz et al., 2009), and the prominence given to the role of dysfunctional beliefs as drivers to pathology (Salkovskis, 1985; Abramowitz et al., 2006), suggesting that additional cognitive components would lead to enhanced treatment results. This finding should be considered with caution as, although we only allocated studies to the cognitive elements group if they had explicitly stated this was part of their procedure, it was not possible to identify how often and to which patients it was delivered. Nonetheless, treatment with cognitive elements resulted in a significant change between pre-treatment to post-treatment, suggesting patients benefitted from it. Further, efficacy of Behavioural Therapy alone and CBT is also reported elsewhere (Öst et al., 2015; Skapinakis et al., 2016).

Our next moderators, hours of therapy and years of OCD duration, were non-significant, meaning that change in YBOCS scores between pre-treatment and post-treatment were unaltered.

Implications

According to these findings, ERP should be considered the treatment of choice for OCD. As treatment-seeking is an issue for patients, ongoing research into the success of treatment is essential in order to first, provide a safe environment where patients feel confident of the opportunity for improvement and second, to increase awareness. Hopefully, continuing to provide consistent results and building on current knowledge will encourage more people suffering to come forward and seek treatment. It is also noteworthy that no studies, but one (Jaurrieta et al., 2008), had an upper limit YBOCS score for inclusion, indicating that even severe cases were included in the trials. Further augmenting the generalisability of our findings, it is notable that the included studies were carried out across 11 countries globally, all contributing to the pool of our significant result.

Our moderator analyses also have valuable implications. Even though ERP with cognitive elements did not surpass 'standard' ERP, its efficacy is notable regardless. Our results could also suggest that benefit from the addition of cognitive elements is dependent on the individual. It has been shown that dysfunctional beliefs play a particularly salient role in certain sub-types of OCD (Abramowitz et al., 2006) and therefore cognitive adjuncts would not aid those with less prominent dysfunctional beliefs. Additionally, attempting to dissociate cognitive techniques completely from ERP delivery may prove difficult, considering discussions around dysfunctional beliefs take place (Abramowitz, Taylor and McKay, 2005) and therapists implement additions to varying degrees during ERP delivery (Jacoby and Abramowitz, 2016).

Next, we demonstrated that hours of therapy did not affect pre-treatment to post-treatment change. The hours of therapy offered in the included studies ranged considerably: from nine to forty and a half hours. This is potentially enormously consequential, as it could suggest that measurable reductions in OCD symptomatology are achievable with less hours, thus putting less burden on public health services or self-funded patients and offering patients faster relief. Although, this should be considered with caution. Last, we found that years of OCD duration also did not affect pre-treatment to post-treatment change; this should be highly reassuring for patients. Years spent with OCD in the studies within our analysis ranged between seven and thirty years, hence our results suggest that ERP can lead to improvements for a whole range of patients.

Limitations

Our study is not without drawbacks, and these should be taken into consideration. The first limitation is regarding treatment protocol ambiguity of adjunct cognitive elements. In the literature this is also evident: some use ERP interchangeably with CBT, thereby including the cognitive aspect (McKay et al., 2015; Öst et al., 2015), and the indistinctness around this is well recognised (Abramowitz and Houts, 2005). Although we performed a moderator analysis specifically to investigate this and paid attention to carefully selecting studies with clear protocols, we cannot be certain about what occurred in every therapy session.

Second, we conducted a risk of bias assessment, and the most critical criteria were met by at least half of the studies (random sequence generation, blinding of outcome data and dealing with incomplete outcome data). As discussed, allocation concealment and blinding of participants and personnel was not strictly possible as studies were assessing psychotherapeutic interventions. A source of potential bias was possibility of selective reporting. Cochrane guidelines indicate this could lead to 'within-study publication bias' (Higgins and Green, 2011). Nonetheless, due to the strength of the literature supporting ERP, we can assume that our results are representing a true treatment effect.

Another limitation was that many studies had small sample sizes, and further, not all conducted a power estimation. This calculation ensures that enough participants are selected in a clinical trial in order to avoid Type I and II errors that mean the true effect of the intervention is overestimated, as with the former, or, in the latter's case, underestimated (Jones et al., 2003). As with other limitations, due to the abundance of literature supporting our findings, we can still consider them to be reflecting a true result.

Next, we did not analyse changes in depression, anxiety and QoL scores. As with our main outcome measure (YBOCS), we wanted to avoid combining different measures in order prevent bias (Morris and Deshon, 2002; Öst et al., 2015). Indeed, a variety of depression, anxiety and QoL were adopted by each study, if any (see Appendix 3 for other outcome scales used by the studies). We therefore opted not to investigate these variables, regrettably because the life of an OCD patient is impacted in a multitude of ways and it is important to observe disease progression as such. As previously discussed, depression (Abramowitz, 2004), anxiety (Nutt and Malizia, 2006) and a decline in QoL (Coluccia et al., 2016) are highly prominent in OCD, hence any therapy should aim to measurably change these too. We also could not

evaluate the long-term treatment effect of the ERP intervention versus the other groups, which would constitute a worthy investigation due to the rates of relapse following treatment interventions which both require further clarification and attention in ensuring patient recovery and well-being. This investigation was not feasible as the majority of studies did not extend measures to include follow-up assessments, a caveat to be addressed by future study designs. Should they have been available, a further review could take place.

Finally, a note on the limitations of RCTs more broadly. Albeit the gold-standard design in research, criticisms of RCTs, particularly in relation to psychological intervention studies, question the generalisability of findings. These include: poor sampling practices, which restrict patient inclusion to those without comorbidities or high severity scores thereby limiting the applicability to the general population; similarity between groups after randomization not being measured with relevant metrics (such as intelligence or cognitive flexibility) but with standard demographic measures; various assumptions including therapy standardisation across patients, to name a few (Shean, 2014; Carey and Stiles, 2015). While considering these limitations, it is noteworthy that various studies included here included patients with comorbidities (eg. Belloch et al., 2008 or Challacombe et al., 2017), all but one had no upper YBOCS score for inclusion and ERP generally is tailored around the individual thereby ensuring a more robust representation of the general population base.

Future directions

A majority of the literature, including this review, supports the efficacy of ERP in consistently reducing OCD symptomatology; future studies and reviews should focus on optimizing the therapy itself by investigating specific elements and how they can impact treatment effect. These could be based on variables that have been related to successful treatment in the literature, which include: *in vivo* and *imaginal* exposure, psychoeducation and relapse prevention (Foa et al., 1980; Abramowitz et al., 2003b; Abramowitz and Arch, 2014; Foa and McLean, 2016). Other variables of interest could include patient prior treatment, session frequency, and initial depression and initial QoL scores (Franklin et al., 2000). Additionally, the treatment effect of additional elements such as those discussed in the rationale, mindfulness-based or family-based ERP, should be explored further individually.

Another intriguing area for further research is to examine the treatment effect of delivering ERP treatment within the two mechanism-of-change frameworks elucidated in the introduction. The literature seems to support an inhibitory learning approach of fear *tolerance* and extinction; delivering ERP within this framework could increase its efficacy (Craske et al., 2008; Craske, 2015). Delivering ERP within an EPT framework which encourages fear *habituation* could also be of interest, although some have suggested this method could create more opportunities for relapse (Abramowitz and Arch, 2014; Jacoby and Abramowitz, 2016). Studies could directly compare these frameworks, in order to decipher which leads to superior and longer-lasting symptom reduction.

Another avenue to yield increasingly consistent treatment effects is to investigate personalised approaches to therapy. This could be implemented at an individual level, investigating a variety of cognitive styles and tailored approaches that focus on the idiosyncratic nature of obsessions and compulsions. Additionally, there could be an increasingly specific approach to OCD subtypes (Abramowitz et al., 2005). This has begun to take place for sub-types which are now considered clinically distinct from OCD such as hoarding, a subset of patients which has been found to response poorly to traditional OCD treatment (Steketee et al., 2010). Furthermore, ameliorating treatment for patients with prominent comorbidities should also be part of the effort in tailoring treatment. Indeed there are successful case studies on ERP for OCD patients with MDD (Abramowitz, 2004) and trials assessing a version of ERP with incorporated therapy for MDD (Rector et al., 2009). More studies investigating other common comorbid disorders, such as affective disorders (Nestadt et al., 2001) are needed.

Concluding comments

Once thought to be rare and intractable, OCD is now recognised as a common disorder with a positive prognosis. Yet, it is also considered to be one of the most devastating conditions with the most complex psychopathology of emotional disorders (Abramowitz, 2006b), therefore it is vital to keep on researching and updating the field. Although pharmacological options are effective and less intensive than psychological interventions, relapse after discontinuation is higher (Simpson et al., 2005), and almost the majority of patients do not benefit (Fineberg et al., 2012). Moreover, it is noteworthy that patients themselves prefer psychological therapy or a combination (Patel and Simpson, 2010). Our results support the evidence for the most popular psychological therapy available, ERP, in that it should be offered

to patients as a reliable and effective treatment. There is still progress to be made, particularly with regards to refining elements of the therapy itself and tailoring to patient's needs; we hope to have contributed to this advancement.

Appendix 1: Additional data extrapolation process

Gomes et al. (2016) provided Standard Errors (SE) from which SD's were calculated using *Equation 1* by multiplying the SE by the square root of the sample size (*N*) in each group:

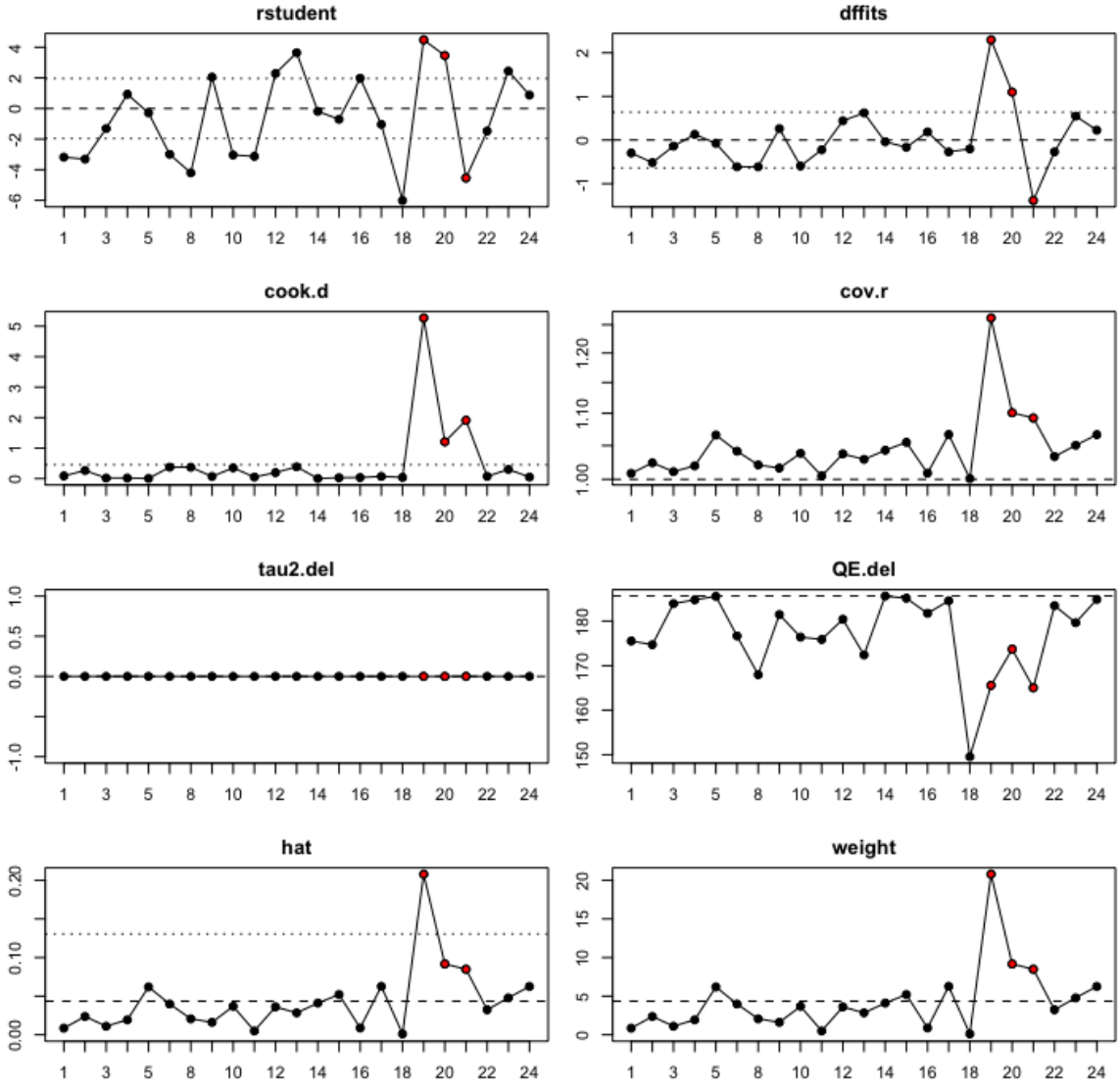
$$SD = SE \times \sqrt{N} \qquad \textit{Equation 1}$$

Visser et al. (2015) provided 95% Confidence Intervals (CI), which were used to calculate SD's, using *Equation 2*.

$$SD = \frac{\sqrt{N} \times (upper\ limit - lower\ limit)}{x} \qquad \textit{Equation 2}$$

As the sample size for this study was small (<60 in each group) *x* represents the SE width of the 95% CI, which can be found in *t* distribution tables with the appropriate degrees of freedom ($N - 1$) for each group. This value is then multiplied by 2 to get *x*. For the treatment group (ERP) this was 4.026; for the other group, Inference-Based Approach (IBA) this was 4.036. Prior to the calculation, it was ensured that the CI was symmetrical to the mean.

Appendix 2: Plots of influential case diagnostics



Plot of the externally standardized residuals, DFFITS values, Cook's distances, covariance ratios, leave-one-out estimates of τ^2 and test statistics for residual heterogeneity, hat values, and weights for the 24 studies included in the meta-analysis comparing ERP treatment versus 'other' groups.

Appendix 3: Scales used to measure depression, anxiety and QoL

Author	Year	Depression Scale	Anxiety Scale	QoL scale
Lindsay et al.	1997	BDI	STAI	Interference Rating Scale
Freeston et al.	1997	BDI	BAI	CFA
O'Connor et al.	1999	BDI	STAI	NA
Cottraux et al.	2001	BDI	FQ	QOL
McLean et al.	2001	BDI	NA	NA
Cordioli et al.	2003	17-HamD	HamA	WHOQOL-BREF
Simpson et al.	2004	HamD	NA	NA
Vogel et al.	2004	BDI	STAI	NA
O'Connor et al.	2005	BDI	BAI	NA
Foa et al.	2005	HamD	NA	NA
Nakatani et al.	2005	17-HamD	HamA	GAF
Fineberg et al.	2005	MÅDRS	HAS	SASS
Whittal et al.	2005	BDI	NA	NA
Sousa et al.	2006	BDI	BAI	WHOQOL-BREF
Anderson and Rees	2007	BDI	NA	Q-LES-Q
Belloch et al.	2008	BDI	STAI-State	NA
Jaurrieta et al.	2008	HamD	HamA	NA
Khodarahimi	2009	NA	NA	NA
Belotto-Silva et al.	2012	NA	NA	NA
Visser et al.	2015	BDI	BAI	EuroQoL
Gomes et al.	2016	BDI	BAI	NA
Challacombe et al.	2017	DASS-Depression	DASS-Anxiety	NA
Fineberg et al.	2018	MÅDRS	NA	EuroQol
Marsden et al.	2018	PHQ-9	GAD-7	WSAS

BDI= Beck Depression Inventory; HamD= Hamilton Rating Scale for Depression; MÅDRS= Montgomery-Åsberg Depression Rating Scale; DASS= Depression Anxiety Stress Scales – Depression; PHQ-9= Patient Health Questionnaire 9; STAI= State-Trait Anxiety Inventory; BAI= Beck Anxiety Inventory; FQ= Mark's Fear Questionnaire; HamA= Hamilton Rating Scale for Anxiety; HAS= Hamilton Anxiety Scale; GAD-7= Generalised Anxiety Disorder Assessment; CFA= Current Functioning Assessment; QOL= Quality Of Life Scale; WHOQOL-BREF= World Health Organization Quality of Life Assessment; GAF= Global Assessment of Functioning, SASS= Social Adjustment and Self-Evaluation Scale; Q-LES-Q= Quality of Life Enjoyment and Satisfaction Questionnaire; EuroQoL= EuroQoL scale; WSAS= Work and Social Adjustment Scale.

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Declaration of Interest:

None.

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